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Ontario

ROYAL COMMISSION OF INQUIRY INTO CERTAIN
DEATHS AT THE HOSPITAL FOR SICK CHILDREN AND
RELATED MATTERS.

Hearing held
21st floor
180 Dundas Street West
Toronto, Ontario

The Honourable Mr. Justice S.G.M. Grange

Commissioner

P.S.A. Lamek, Q.C.

Counsel

E.A. Cronk

Associate Counsel

Thomas Millar

Administrator

Transcript of evidence
for

June 6, 1984.

VOLUME 150

OFFICIAL COURT REPORTERS

Angus, Stonehouse & Co. Ltd.,
14 Carlton Street, 7th Floor,
Toronto, Ontario M5B 1J2

595-1065



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DEATHS AT THE HOSPITAL FOR SICK CHILDREN
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Hearing held on the 21st Floor,
180 Dundas Street West, Toronto,
Ontario, on Wednesday, the 6th
day of June, 1984.

- - - -

THE HONOURABLE MR. JUSTICE S.G.M. GRANGE - Commissioner
THOMAS MILLAR - Administrator
MURRAY R. ELLIOT - Registrar

APPEARANCES:

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L. CECCHETTO)	General and Solicitor General
		of Ontario (Crown Attorneys
		and Coroner's Office)
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M. THOMSON)	Sick Children
R. BATTY)	
D. YOUNG)	Counsel for the Metropolitan
		Toronto Police
W.N. ORTVED)	Counsel for numerous Doctors
K. CHOWN)	at the Hospital for Sick
		Children
F. KITELY)	Counsel for the Registered
		Nurses' Association of Ontario
		and 35 Registered Nurses at
		The Hospital for Sick Children



APPEARANCES: (Cont'd)

D. BROWN)	Counsel for Susan Nelles - Nurse
G.R. STRATHY)	Counsel for Phyllis Trayner - Nurse
P. RAE)	
J. OLAH)	Counsel for Janet Brownless - Nurse
S. LABOW)	Counsel for Mr. & Mrs. Gosselin, Mr. & Mrs. Gionas, Mr. & Mrs. Inwood, Mr. & Mrs. Turner, Mr. & Mrs. Lutes, and Mr. & Mrs. Murphy (parents of deceased children)
W.W. TOBIAS)	Counsel for Mr. & Mrs. Hines (parents of deceased child Jordan Hines)
J. SHINEHOFT)	Counsel for Lorie Pacsai and Kevin Garnet (parents of deceased child Kevin Pacsai)

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I N D E X

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(ii)

E R R A T A

June 4, 1984

PAGES 107 to 109 MR. YOUNG should read MR. HUNT

48 to 55 MR. BROWN should read MR. STRATHY



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---On commencing at 10:00 a.m.

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THE COMMISSIONER: Yes, Miss Cronk?

4

MS. CRONK: Good morning, sir. I am not sure whether to welcome everybody back to Pharmacology 404 or not, sir, but I would like to continue from where we left off yesterday.

5

6

7

THE COMMISSIONER: Yes.

8

ARGUMENT BY MS. CRONK

9

MS. CRONK: You will recall at the end of the day we were about to turn to the consideration of the actual measurements of digoxin that had been measured in the various tissue and blood specimens taken from some of the 36 children.

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There are, however, a number of technical matters concerning the results that were achieved and how they were reported that are in my submission fundamental to understanding exactly what Mr. Cimbura has said in his reports. First, sir, his distinction as you will recall between the type of specimens that was tested at the Hospital for Sick Children as opposed to the type of blood specimen that was tested at the Centre of Forensic Science.

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At the Hospital digoxin assays run on, at that time only RIA, were run on serum or plasma samples. Mr. Cimbura has testified that whole blood for forensic purposes is preferable, and whenever



1
2 possible it was that type of specimen in respect of
3 which he ran his assays.

4 You recall, sir, that whole blood has
5 been described by him really as a mixture containing
6 the red blood cells that might otherwise be extracted
7 in the process of refining whole blood to serum or
8 plasma.

9 Two other distinctions: at the Hospital
10 when RIA assays were run on either serum or plasma
11 they did so - I am sorry, if a sample of whole blood
12 was provided they in fact centrifuged it to ensure
13 that what they in fact tested was either serum or
14 plasma. Mr. Cimbura on the other hand took the sample
15 of whole blood as it came in to him but ran an
16 extraction process on it first and then ran his
17 assays.

18 THE COMMISSIONER: What did he extract?

19 MS. CRONK: The purpose of that, as
20 I understood it, was to ensure that there was a
21 component of red blood cells left in the sample, but
22 it was intended to eliminate as much of the fluid
23 components of the body as might be in the specimen.

24 The circumstances surrounding the test-
25 ing of tissues differs as well, depending on whether -
I'm sorry?



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THE COMMISSIONER: I know I had this
before but blood is composed of what?

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MS. CRONK: Whole blood is a composition
including red blood cells, sir.

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THE COMMISSIONER: All right. Yes, I
am sure it has red blood cells. How do you make up -
what is the difference between serum and plasma and
blood?

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MS. CRONK: As I understand it, sir, and
my friends can correct me if I am wrong, the plasma
sample has the red cells. There is a coagulant that
has been added to it so that the red blood cells are
no longer present whereas they are present in serum.

14

Whole blood is the original sample
as you would draw it directly from the body.

15

16

THE COMMISSIONER: In plasma the red
blood cells are eliminated and?

17

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MS. CRONK: And in serum they are
present.

19

MS. RAE: If I could be of assistance?

20

THE COMMISSIONER: Yes. I had this
all out before.

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23

MS. RAE: If you prevent the blood
clotting by using an anticoagulant and then spin down
the red blood cells you are left with plasma.

24

25



1
2 THE COMMISSIONER: Would you say that
3 again? Prevent clotting?

4 MS. RAE: Prevent clotting by using
5 an anticoagulant which is a chemical you add to blood,
6 and then you centrifuge.

7 THE COMMISSIONER: And then?

8 MS. RAE: You remove the red blood
9 cells and you are left with plasma.

10 THE COMMISSIONER: Yes.

11 MS. RAE: The liquid that is left is
12 plasma which contains no red blood cells. On the
13 other hand --

14 THE COMMISSIONER: I understand that.
15 Plasma has no red cells but what then is serum?

16 MS. RAE: If on the other hand you
17 do not add the anticoagulant and you let the blood
18 clot --

19 THE COMMISSIONER: Yes.

20 MS. RAE: - and then spin it, you
21 remove the red blood cells and certain of the plasma
22 proteins and the liquid you are left with is serum,
23 but there are again no red blood cells in it.

24 MS. CRONK: I think, sir, I get five
25 marks on the plasma and no marks on the serum.

THE COMMISSIONER: I think I get zero



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on both.

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MS. CRONK: The other distinction I
submit --

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THE COMMISSIONER: Miss Rae, you have
got a teacher's certificate, have you?

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MS. CRONK: On this exam, sir, that
is certainly true.

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The other distinction of some signifi-
cance in my submission, sir, relates to tissue
specimens. You will recall that the evidence has been
that no tissue specimens were assayed at all at the
Hospital for Sick Children except in a very limited
experimental sense following the death of Justin Cook.
Dr. Ellis originally at the request of the Metropolitan
Toronto Police Force did undertake on what he has
described as a purely preliminary and experimental
basis some tissue assays. That was the first time
it had been done, and it wasn't done according to the
evidence before you, subsequently.

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Obviously many of the specimens tested
at the Centre of Forensic Sciences were in fact tissue
specimens of varying nature. Mr. Cimbura has described
for you the process that was designed at the Centre
and tested before assays were run on tissues, and it
was really a four step process, sir.



1
2 When the specimen first came in it was
3 weighed, cut and then liquefied. That has also been
4 described as homogenization. Obviously, sir, it is
5 the fluid that is used for the assay purposes so the
6 tissue specimen had to be converted or transposed to
7 that form before the assay could be conducted.

8 The second step was that he then
9 performed an extraction process utilizing an organic
10 solvent designed to purify the sample.

11 You will recall, sir, that there has
12 been a great deal of evidence concerning so-called
13 recovery studies conducted by Mr. Cimbura and his
14 colleagues. Those studies in this context relate to
15 this extraction process used on tissues. The purpose
16 of the study, sir, is to determine how much of the
17 digoxin concentration is in fact lost from the tissue
18 specimen during the extraction process.

19 It was Mr. Cimbura's evidence that
20 his laboratory ran a series of tests and they found
21 that approximately 85% of the digoxin concentration
22 in the specimens was retained; was not lost.

23 The details of those studies, sir, are
24 set out in Exhibit 213 at pages 1 through 4, and in
25 particular page 2.

After the extraction process had then



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been completed on the specimen, sir, Mr. Cimbura then performed an RIA assay on the specimen using we know a double antibody RIA system. The first purpose of one of the types of antibodies was obviously to attract the digoxin in a binding sense, and the second type of antibody in the system was to act as a filtration device or a separation technique.

Then finally the very last step that he used from the late summer of 1981 and the fall of 1982 his laboratory was in a position to then utilize --

THE COMMISSIONER: I am sorry, you said from the?

MS. CRONK: From the late summer of 1981.

THE COMMISSIONER: Until?

MS. CRONK: Until the early fall of 1982. From that point forward --

THE COMMISSIONER: I am sorry, you don't mean that, do you? The late summer is not followed by the early fall next year.

MS. CRONK: I'm sorry, sir, you are quite right. The late summer and fall of 1981, sir. You are quite right. Thank you.

The laboratory was then in the position



1
2 to use the HPLC technique coupled with RIA that had
3 been modified at the Centre of Forensic Sciences so
4 that these assays could be run.

5 Mr. Cimbura's evidence was that tissue
6 specimens had not with great frequency in the past
7 been tested on digoxin assays; that his laboratory
8 was required to design a procedure that would permit
9 that, and that that was really effectively completed
10 only in the fall of 1981. From that point forward
11 specimens that were made available to him had the benefit
12 of the RIA plus HPLC and RIA technique. The ones
13 that came in earlier than that were submitted to
14 RIA only, unless there was specimen left and they
15 were then re-assayed when the HPLC technique had been
16 perfected.

17 There is one other technical aspect
18 of the matter, sir. You will recall that we heard
19 evidence concerning something called a minimum
20 detection level on these assays. That has been
21 described by the biochemists who have appeared before
22 you as really a lowest measureable concentration below
23 which it can't be said with any satisfactory degree
24 of scientific certainty that the test results clearly
25 indicate digoxin. It is in fact, sir, in perhaps
a layman's language, the lower cut-off line.



1
2 At the Hospital for Sick Children on
3 the RIA during the enquiry period the cut-off was
4 .2 nanograms per millilitre. In January 1982 for
5 reasons that in my submission are not particularly
6 germane at this stage that minimum was raised to
7 0.5 at the Hospital.

8 During the same period of time at the
9 Centre of Forensic Sciences the minimum detection
10 level was regarded as 1 nanogram per millilitre.
11 Mr. Cimbura, however, testified that in his judgment
12 and experience the assay that was being used at the
13 Centre was in fact capable of measuring to as low as
14 .5 nanograms, but the readings below 1 in his judgment
15 for forensic purposes were not significant so he used
16 the level in virtually all instances a cut-off of
17 1 nanogram.

18 We have heard evidence as well, sir,
19 about the maximum detection or measurable point beyond
20 which dilution will be required to further assay
21 the sample. Again dealing with the Hospital first
22 during the enquiry period the measurable concentration
23 on RIA was 4.7 nanograms or 5 nanograms per millilitre.
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B-1

RD/ac

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MS. CRONK: You may recall, sir, that there was some confusion in Dr. Ellis' testimony, as to whether the number was, in fact, 4.7 or 5. Various in the digoxin books it is recorded as being 4.7 or 5. The clear point on it, sir, is simply that any level, any reading of greater than 4.7 or 5 required further dilution of the sample before an exact fix on the concentration could be provided. At the Centre for Forensic Sciences, the RIA equipment was as calibrated at the upper end of the scale at 6 nanograms per millilitre. Anything beyond that required further dilution for a fixed measurement.

At the Centre, when Mr. Cimbura ran these tests, sir, you will recall from having reviewed his report and having heard his evidence that there were three different kinds of tests run. In some cases only the RIA procedure was used. On some specimens a combination of RIA plus HPLC, followed by another RIA assay was used. There is a variation even on that one, sir. Effectively, Mr. Cimbura has said that there were some instances where he ran RIA three times, plus HPLC on the same specimen type.

Then, as I mentioned yesterday, sir,



B-2

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2 in three cases that RIA/HPLC/RIA combination was
3 supplemented by gas chromatography or mass
4 spectrometry. We will come to those three specific
5 cases.

6 There is, as well, sir, a further
7 aspect of Mr. Cimbura's reports, that is, in my
8 submission, a fundamental significance and that is
9 the way in which he expressed the results, and I
10 think this is a matter of sufficient concern, sir,
11 that I would ask you to look, if you would, please,
12 at Exhibit 95 which is the bundle of reports
13 prepared by Mr. Cimbura.

14 THE COMMISSIONER: I have it.

15 MS. CRONK: Could I ask you to
16 look, sir, first, if you would look, please, at
17 Exhibit 95A, which is the first report dated
18 January 11, 1982, and I would ask you to turn to
19 page 2.

20 The purpose of this exercise, sir,
21 as you will recall Mr. Cimbura used four different
22 kinds of expressions of language, if you will, to
23 describe his results. The language that he used,
24 with respect to each specimen, indicates the type
25 of analytical technique to which the specimen was
subjected. From my submissions yesterday, sir,



B-3

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2 you will readily appreciate that in situations
3 where the HPLC and RIA technique was undertaken
4 it was Mr. Cimbura's opinion that he had isolated
5 and measured pure digoxin. It, therefore, becomes
6 of great significance, in my submission, to
7 understand precisely which specimens were subjected
8 to that procedure, as opposed to RIA only.

9 By purposes of illustration, sir,
10 there appear to be four different types of
11 expression of result. I would ask you to look
12 first, if you would, at T11, sample no. T11 (a),
13 dealing with the heart: ventricular. This
14 happens to be a result on Justin Cook -- I'm sorry,
15 if we could look at the left atrium on Justin
16 Cook you will see that the results were expressed
17 in this way:

18 " The tissue was found to contain
19 39 ng/g (calculated as digoxin)
20 of digoxin and/or digoxin-like
21 substance(s). "

22 You will see that that phrase is repeated in a
23 number of, in respect of a number of samples
24 throughout the report, Mr. Commissioner. Mr. Cimbura
25 has testified that that language means that the
assay was run using RIA only.



B-4

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Mr. Cimbura thus did not know whether he was recording dixogin or dixogin-like substances or, indeed, Substance X or a combination of the three.

The second example, sir, is the very next one, the results on the septum tissue specimen where the results are expressed:

" The tissue was found to contain 36 ng/g (calculated as digoxin) of a mixture of digoxin and digoxin-like substance(s). "

So far it is identical to the one we just looked at, but the following sentence is added:

" The concentration of digoxin was 4 ng/g. "

Use of that language, sir, Mr. Cimbura has said, means that he ran RIA then HPLC and RIA and the results were different, that is on RIA he obtained one reading and then when he did HPLC and RIA separately on the specimen he got another reading and the results were different. He concluded, therefore, he has testified that not only the digoxin was present but also digoxin-like substances and he therefore separated the results out to express



B-5

1
2 his findings by RIA only and then by HPLC and RIA.
3 He believed, of course, that the results that he
4 was getting on HPLC and RIA were pure digoxin.

5 So, to interpret that kind of
6 language, sir, in light of Mr. Cimbura's evidence,
7 it would appear that the pure RIA reading was
8 36 nanograms per gram. That was a mixture of
9 what Mr. Cimbura believed to be digoxin and potentially
10 digoxin-like substances. The reading that he felt
11 to be a pure digoxin measurement was the result of
12 HPLC and RIA and that was 4 nanograms. So for
13 the purposes in those cases where that language
14 is used for the purpose of understanding what his
15 actual digoxin measurement was, it is the second
16 figure which is of significance, in my submission.

17 The third example, sir, if I could
18 ask you to turn to page 11 of the same report. If
19 you could look to the specimens concerning Amber
20 Dawson no. T35, at this time dealing with the left
21 ventricle. You will see that the results in this
22 case are expressed as follows:

23 " The tissue was found to contain
24 19 ng/g (calculated as digoxin)
25 of digoxin-like substance(s). "

And then:



B-6

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" No digoxin could be detected. "

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Obviously, sir, there is an apparent difference

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in language. Mr. Cimbura has explained that that

5

kind of language means, once again, that he did

6

both an RIA assay and an HPLC and RIA assay, but

7

the results on both were negative. I'm sorry,

8

the results on the HPLC and the RIA were negative,

9

so he has reported the RIA result, which again

10

is the one that may include digoxin-like substances,

11

but his statement that no digoxin was present was

the reflection of the HPLC/RIA results.

12

And then finally, sir, I will

13

ask you to go back to page 1, the same report. Any

14

of the three examples set out on this page, sir,

15

reflect the fourth category of finding, if you will.

16

If we could deal, for example, with the heart muscle,

sample no. T42:

17

" The tissue was found to contain

18

1,177 nanograms per gram (ng/g)

19

of digoxin. "

20

Mr. Cimbura has testified once again that that

21

means that both RIA and HPLC and RIA techniques

22

were used.

The results were both positive and

23

both consistent. The two were corroborative in

24

his opinion of one another. He concluded, therefore,

25



B-7

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2 the concentrations measured were pure digoxin.

3 There is one other aspect of
4 Mr. Cimbura's report, sir. Again, it is necessary
5 to be fully understood, as you will recall, in
6 order to understand even the threshold of
7 significance of the results and that is the ranges
8 expressed by Mr. Cimbura as being representative
9 of cases where patients were on therapeutic doses
10 of digoxin and ranges reported in tissue specimens
11 in cases reported in the literature as having been
fatal poisoning cases.

12 I have prepared, sir, a chart which
13 sets out the ranges that Mr. Cimbura included in
14 his report. It has been provided to Counsel. It
15 may be easier, sir, in going through Mr. Cimbura's
results, to have this before you.

16 You will see, sir, that Mr. Cimbura
17 set out ranges in five different contexts. The
18 first was with respect to blood or serum levels in
19 children on digoxin therapy, that is the therapeutic
20 range and on children in fatal poisoning cases,
21 that is the toxic or fatal range. Similarly he
22 set out a range with respect to heart muscle, lung
23 tissue, liver tissue and then fresh autopsy
24 specimens. All of these ranges, sir, are set out
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B-8

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in Exhibit 95 at various places. It may be more
convenient for everybody to have it in one place,
as we actually examine the numbers.

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C-1

DM/hr

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2 In contrast the toxic or fatal poisoning range at
3 which he set out were drawn from what he described
4 as the published results of forensic toxicologists
5 in past cases of investigated digoxin poisoning and
6 as well from research conducted at the Centre of
7 Forensic Sciences.

8 In support of what he believed to be
9 the appropriate ranges as reflected by the literature,
10 Mr. Commissioner, with respect to blood specimens,
11 Mr. Cimbura as well did a specific study at the Centre
12 to determine whether or not the concentrations of
13 digoxin in blood specimens were different depending
14 upon the site in the body from which the sample had
15 been taken. The results of that study, sir, are
16 before you in Exhibit 213-7. The results demonstrated
17 that post mortem levels in samples of sagittal sinus
18 blood and eye fluid were lower than post mortem levels
19 of digoxin measurable in heart blood.

20 Of particular note, sir, with respect
21 to these ranges, none of the pharmacologists who
22 testified before you challenged the appropriateness
23 of the ranges for tissues, and in particular, for
24 example, heart muscle as set out by Mr. Cimbura.
25 Accordingly in my submission on the evidence these
ranges must be accepted as reasonable expressions of



C-2

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2 toxic and therapeutic ranges found in post mortem
3 specimens --

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THE COMMISSIONER: But there are so
5 few of them, that is the problem, if you get one
6 more it might well be possibly lower.

6

MS. CRONK: I am sorry, sir.

7

THE COMMISSIONER: There are so few
8 of his examples, are there not, perhaps I am wrong?

9

MS. CRONK: I am not sure that I
10 am understanding you, sir.

10

11

THE COMMISSIONER: There are so few
12 cases that he has referred to, in some cases it is
13 just one, sometimes two or three.

13

14

MS. CRONK: In the case of fresh
15 autopsys specimens, sir, you will see certainly that
16 is the case, he has referred to seven specific cases.
17 But in a different context each of the pharmacologists
18 for example, Dr. Spielberg when he testified, was asked
19 whether or not on the basis of his own review of the
20 literature and his own review of reported cases he
21 would quarrel with these ranges, and his evidence,
22 sir, was that he would not specifically with respect
23 to the ranges for fresh heart.

21

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THE COMMISSIONER: I wasn't quarreling
23 with what you said there, I was only quarreling with

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C-3

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the conclusion that you had reached that I have to accept them. I don't have to accept them unless they appeal to me as making some kind of sense. If there are only three or four and if the range is enormous then perhaps I can assume if they had seven or eight the range would be even larger.

MS. CRONK: I'm sorry, sir. If I may attempt to be clearer. It is my submission that they should be accepted by you as reasonable ranges recognizing two caveats. The first is that there is this tremendous area of overlap that all of the pharmacologists agree applies, so that a specific measurement in any given individual may fall both within the therapeutic end of the toxic range, but in a particular patient reflect toxicity and in another patient reflect nothing more than a therapeutic level with no sign of digoxin toxicity and no suggestion that digoxin has contributed to the death of the individual, that is the first caveat.

Second, sir, is exactly what you suggest that is again as recognized by all of the pharmacologists this tremendous potential for individual variability. So that although numbers have been reported in the literature as being within, as establishing a fatal poisoning range or a number which



C-4

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exemplifies a fatal poisoning case, we must recognize that there is this potential for tremendous variability from individual to individual, and those really are the caveats, sir, that all of the pharmacologists placed on these ranges.

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9

THE COMMISSIONER: All I was trying to do was put on another caveat that is the tremendous variability maybe even more tremendous when we get more examples.

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MS. CRONK: I quite agree, sir, I quite agree, sir. Given the ranges that Mr. Cimbura was in fact dealing with based on the research that had been conducted at the Centre and what he had read in the literature, he reported levels of digoxin within the toxic or fatal range on 12 children on selected samples. These were Justin Cook, Kevin Pacsai, Allana Miller, Kristin Inwood, Jordan Hines, Colleen Warner, Charlon Gardner, Jennifer Thomas, Matthew Lutes, Stephanie Lombardo, Barbara Gionas and Jessie Belanger.

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As you know, sir, Commission staff have prepared charts of Mr. Cimbura's various results. We did so for two reasons. First in many cases the ante mortem and post mortem blood levels, at least there is data particular to those kinds of specimens



C-5

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2 available from the Hospital for Sick Children, and
3 hence were not included in Mr. Cimbura's report
4 unless also tested there.

5 Secondly, Mr. Cimbura filed six
6 reports over the course of time and the results
7 particular to each child in some cases appeared in
8 a number of reports, the hope is that this would
9 simply make it a matter of easier reference.

10 As well, sir, there are certain
11 features in the chart, and I believe you have a copy
12 as do other counsel, that I would point out. The
13 first is when we come to deal with Justin Cook, if
14 you could turn to the second page of Justin Cook
15 dealing with tissue specimens you will see a column
16 entitled, "comments" and although that might be
17 a misnomer by any other name, the column is intended
18 to record which technique was used by Mr. Cimbura
19 for particular specimens. All we have really done,
20 sir, is take his expression of language of results
21 and converted it into a type of technique that he
22 used.

23 If we could start then sir with the
24 case of Justin Cook. You will recall, of course that
25 there were a number of blood or serum or plasma
specimens available both from the Hospital for Sick



C-6

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2 Children and as tested at the Centre of Forensic
3 Sciences. It is not my intention to go through each
4 of the results on all of these children in any detail.
5 I would however, make the following observations with
6 respect to the results on Justin Cook.

7 You will note that the blood specimens
8 tested at the Hospital for Sick Children which resulted
9 on post mortem specimens in a level of 68 nanograms
10 on one sample and greater than 100 nanograms on
11 another sample, were tested by use of RIA only. The
12 ante mortem blood sample tested at the Hospital for
13 Sick Children resulted in a level of 72 nanograms.
14 The evidence of Dr. Soldin has been that that
15 particular sample was assayed five times to produce
16 the level of 72. The post mortem blood sample tested
17 at the Hospital for Sick Children, were in fact two
18 of them, drawn at autopsy by Dr. Cutz, the one with
19 which I am particularly concerned is sample number
20 D 57978, that is the one, sir, that resulted in a
21 level of greater than 100 nanograms. That specimen
22 Dr. Soldin has said was assayed on several dilutions
23 on March 22, that is when the reading of greater than
24 100 was achieved. It was however re assayed again from
25 scratch on several dilutions by Dr. Ellis on March the
26 24th as a cross-check and the results again were in



C-7

DM/hr

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the order of 100 or greater. Both Dr.'s Ellis and Soldin have testified that they were satisfied that the assays that had been conducted on those specimens at the Hospital were conducted properly and that the results were analytically reliable.

The post mortem autopsy specimen that was tested at the Centre of Forensic Sciences you will see, sir, was tested using RIA plus HPLC and RIA. It is a little bit difficult to read on this chart, sir, but it is the one that resulted in a reading of 91 nanograms per millilitre, set out on page 1, and it is the first specimen shown to have been tested at the Centre of Forensic Sciences, there is an X in the Centre of Forensic Sciences column.

THE COMMISSIONER: Yes.

MS. CRONK: That specimen was an autopsy blood specimen, it was in fact part of the specimen drawn by Dr. Cutz resulting in a level greater than 91 using HPLC and RIA, part of the same specimen was tested at the Hospital using only RIA and resulting in a level of greater than 100. The concentrations found in that post mortem blood specimen then in my submission are corroborative of one another in the sense of the range or the magnitude of the levels that were recorded. Of particular significance of course



C-8

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2 is the HPLC extraction technique was used by Mr.
3 Cimbura and he believed therefore that the 91 nanograms
4 that he had measured was pure digoxin. Quite apart
5 from the testing of that sample at the Hosptial and
6 at the Centre of Forensic Sciences, however, sir,
7 Mr. Cimbura also arranged for assays to be run at
8 the Toronto General Hospital. The results of those
9 assays as well were within the same level of magnitude
10 on the specimens as were the results of the Centre
according to Mr. Cimbura's evidence.



D-1

EMT/ac

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In addition an important feature of the level quite apparently, sir, is that all of the results on that post mortem blood specimen were within the range of concentrations reported in cases of fatal poisoning as set out by Mr. Cimbura.

In consequence on that post mortem specimen three different laboratories using two different antibody RIA assays and using two different overall types of techniques had achieved results that were essentially corroborative of one another.

I would ask you, sir, if you would for a moment, please, turn to Exhibit 400. I draw your attention, sir, to page 3. You will recall, sir, that Exhibit 400 are the Minutes from the meeting of the panel of experts on digoxin called by the hospital and held here in Toronto on March 19th of this year. Paragraph 5(2) is the paragraph in which certain of the conclusions of the panel participants were set out and in which they indicate that they placed a high degree of confidence in the HPLC/RIA technology. They indicate that this confidence was strengthened on learning of the way in which the HPLC/RIA had been applied. They then make this comment:

" It was noted that in one case, Cook,



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plasma samples had been analyzed
in three different laboratories
using two different antibodies
with reasonable agreement with
respect to results. "

Those are the assays to which I have just referred
you, sir.

THE COMMISSIONER: Yes. Thank you.

MS. CRONK: There was as well a
number of observations with respect to the measure-
ments made in tissue specimens on Justin Cook,
Mr. Commissioner. That is the very next page in the
bundle.

If I could explain how these charts
are intended to work, sir, in the very first column
the type of specimen is set out, and after the
nature of the specimen is described, immediately
below it you will see an indication as to whether
or not it was a fixed tissue specimen, a fresh tissue
specimen or in the cases where it applies an exhumed
or exhumed and ~~emb~~almed tissue specimen. Then of
course the concentration that was measured is set
out.

Where Mr. Cimbura expressed two
numbers (that is a number that was the result of RIA



D-3

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2 only plus a number that was the result of the
3 HPLC/RIA process) only the number which he took to
4 reflect pure digoxin has been **set out** in the
5 column. Then of course the type of analytical
6 technique is set out.

7 If we could deal with the fresh
8 tissue results first, sir, one of the most significant
9 findings in the case of Justin Cook as you are aware
10 is that Mr. Cimbura found toxic levels of concentrations
11 of what he believed to be digoxin in the heart and
12 the lung on fresh tissue specimens from Justin Cook.
13 The tests on both of those specimens was done
14 utilizing HPLC and RIA. The second feature, sir, is
15 that the level in the fresh heart muscle which is
16 reported as 1177 is in fact at the upper end of the
17 range reported in fatal poisoning cases according
18 to Mr. Cimbura's ranges. You recall, sir, that the
19 upper range is 1240 as reported in the literature.

20 The level in the fresh lung specimen
21 was in fact 50% higher in Justin Cook than the
22 maximum values seen to be reported in the literature.
23 I say that, sir, because if you look at the toxic
24 fatal ranges for lung tissue the upper limit quoted
25 in Mr. Cimbura's ranges is 100 whereas the pure
digoxin reading according to Mr. Cimbura on Justin



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Cook's lung tissue is 153.

THE COMMISSIONER: Yes.

MS. CRONK: If we could look then, sir, as well to the fixed tissues in the case of Justin Cook you will see the concentrations of pure digoxin, I'm sorry, it is on the same page, sir.

THE COMMISSIONER: Yes. They are contained somewhere in 95A but where do I find -

MS. CRONK: The ranges, sir, or the results?

THE COMMISSIONER: Cimbura's ranges.

MS. CRONK: All right. The ranges with respect to - remember, sir, I have given you a chart?

THE COMMISSIONER: Yes.

MS. CRONK: And it tells you on the righthand side of the page where in Mr. Cimbura's report it is to be found.

THE COMMISSIONER: Yes. Thank you.

MS. CRONK: It may be helpful, sir, to have the two together as we go through these.

If I could, sir, then just again refer to the point I just made: that is that the level in the fresh lung tissue is in fact 50% higher in Justin Cook than the upper limit quoted in the



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toxic range by Mr. Cimbura for lung tissue. The range in the heart muscle, again fresh tissue, is very close to the upper end of the range that he quoted. He quoted an upper end of 1240 nanograms. The level was in fact as he measured it 1177. That would give you an idea of the order of magnitude of the measurements that were recorded on those two fresh tissue specimens from Justin Cook.

If we could turn then to the fixed -

THE COMMISSIONER: You are now referring to the heart tissue, and the lung tissue - the lung tissue concentration is 153 -

MS. CRONK: Yes.

THE COMMISSIONER: Which is not only greater than therapeutic but is greater than fatal poisoning

MS. CRONK: By 50%, that's right, sir.

THE COMMISSIONER: On that fatal poisoning range, the maximum is only the maximum reported.

MS. CRONK: Exactly.

THE COMMISSIONER: Looking at heart muscle, the concentration found is 1177. That is above the therapeutic range, is it not?

MS. CRONK: Well above the therapeutic



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range, sir. You will see that the therapeutic range quoted is 49 to 975 nanograms.

THE COMMISSIONER: Yes.

MS. CRONK: And the toxic range is 108 to 1240 and I say only with respect to that level, sir, that it is very close to the upper range quoted in the toxic range. It is above the therapeutic and it is towards the upper end of the fatal range as reported by Mr. Cimbura.

THE COMMISSIONER: Yes.

MS. CRONK: Recognizing limitations again of what in fact has been reported in the literature. It is a very high reading, sir.

If we could move then to the fixed tissue specimens, sir, you will see that there was as well a fixed lung specimen. That is item no. 4 on your chart.

THE COMMISSIONER: Yes.

MS. CRONK: And that as well was measured using RIA and HPLC and RIA, and I would point out, sir, the level here, 15 nanograms, is both within the therapeutic range and the toxic range. It therefore is an example of a measurement that falls within this area of overlap that is clearly established by the ranges.



D-7

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THE COMMISSIONER: Yes.

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MS. CRONK: And of course, sir, I need not repeat that all of the levels measured on Justin Cook that are recorded as pure digoxin are measurements on a child that was never thought and was never prescribed digoxin during life.

If we could turn to the next case, Allana Miller, sir, if we could deal first with the blood in serum samples. They are set out on the first part of the page.

You will see, sir, there are really three specimens. This is the only data available to us, and I should say, sir, that in cases where children had been hospitalized for lengthy periods during their life and where there were any number of digoxin ante mortem blood readings available, we have listed on these charts only those available within the last two weeks of their life.

Now in the case of Allana Miller her ante mortem reading on the 19th of March, two days before she died was .6 nanograms per millilitre: clearly well within the therapeutic range. That was tested on RIA.

Two autopsy assays were run, two autopsy specimens. The first at the Hospital for



D-8

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2 Sick Children on RIA only, resulting in a reading of
3 78 nanograms. The second at the Centre for Forensic
4 Science on RIA only, resulting in a reading of 69
5 nanograms.

6 The levels as recorded by both
7 laboratories recognizing that it is RIA only are well
8 within the toxic range and essentially I suggest,
9 sir, there is no material quantitative difference
10 between the two readings given the magnitude of
11 the numbers.

12 Dr. Soldin has testified that the
13 post mortem blood specimen tested at the Hospital for
14 Sick Children was assayed six times on March 21st
15 resulting in levels of greater than 50. At that time,
16 however, the computer projected an actual level
17 somewhere in the 70's. March 21st was a Saturday
18 you will recall, sir. The next morning the sample
19 was assayed again and that is when the result of 78
20 nanograms was in fact realized.

21 The importance of the numbers of
22 assays, sir, that were done is this: Dr. Soldin has
23 testified that in his opinion the greater the number
24 of dilutions and the greater the number of times of
25 repeat assays, the more confidence he can place in
the reliability of the analytical procedure used.



D-9

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2 The point here, sir, is the actual level of 78 was
3 fixed as of the Sunday. Dr. Soldin personally
4 reviewed all of the assays that had been done and
5 the results, the actual calculations, and had
6 satisfied himself that the assays had been performed
7 correctly.

8 At the same time as the assays were
9 being run on the Saturday on the post mortem samples,
10 sir, Dr. Soldin arranged for a sample of oral digoxin
11 elixir from the ward to be assayed to determine if
12 there was any error in the concentration of the
13 preparation itself that had been on the ward.

14 As a result of the tests that were
15 done he concluded that the concentration of digoxin
16 in the preparation of elixir was as it was stated to
17 be. Dr. Soldin's evidence with respect to those
18 assays, sir, are in Volume 50, commencing at page 1289.

19 If we could look then at the fixed
20 tissue specimens in Allana Miller, sir, about which
21 of course you have heard a great deal of evidence it
22 is immediately apparent from the levels that Allana
23 had very small quantities of pure digoxin in her
24 fixed heart tissues described by Mr. Cimbura as
25 traces only of pure digoxin, using again the RIA,
HPLA and RIA method.



D-10

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2 He in fact got readings as I recall
3 it of approximately 4, 5, 7 nanograms on RIA only,
4 but using HPLC only traces were measurable.

5 She had none at all, sir, that was
6 measurable in her fixed lung tissue after HPLA and
7 RIA had been performed on a specimen.

8 The other issue that arises with
9 respect to Allana Miller's levels is of course the
10 issue about which I previously made submissions,
11 and that is whether or not they can be explained as
12 is the theory of Dr. Spielberg on the basis of
13 resuscitation trauma necrosis to tissues during
14 life so as to result in an elevated post mortem
15 blood level.

16 If we could turn, sir, then to the
17 next case, that of Charlon Gardner who died on
18 March 18th, there are no blood or serum specimens,
19 sir, be they ante mortem or post mortem that are
20 available in this case. The only measurements
21 available relate to fixed tissues, heart and lung.

22 You will note, sir, that her fixed
23 heart and lung tissues again were all assayed using
24 the HPLC technique, both the lung and the heart, and
25 the levels thus shown were considered by Mr. Cimbura
to be recordings of pure digoxin.



D-11

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2 The levels in her heart tissue from
3 the ventricle and the septum, sir, are within
4 Mr. Cimbura's toxic range as is the level from the
5 lung tissue. The level from the left atrium, however,
6 is not: it is in the therapeutic range.

7 Mr. Cimbura estimated that the
8 concentrations found in the fixed heart tissue were
9 lower than the actual values that were present in
10 fresh heart tissue before they were placed in
11 preservative. Now you recall, sir, that Mr. Cimbura
12 undertook where possible estimates in an attempt to
13 extrapolate the measurements in fixed tissue back to
14 what the actual level would have been in fresh tissue
15 of a similar type. I mean that if Mr. Cimbura as
16 he did in this case obtained a specimen of fixed
17 heart tissue and got a reading on the left ventricle
18 of 141 which was in the toxic range, he then undertook
19 his procedure of measuring the amount in a fixative
20 solution - you will recall, sir, I outlined the steps
21 he used, referring to the original weight of the
22 organ at autopsy --

23 THE COMMISSIONER: Yes.

24 MS. CRONK:--In an attempt to arrive
25 at an estimate. In certain situations he was able
to pinpoint an actual number, an actual measurement



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he thought may have existed in fresh tissues. In other cases, he was not. In this case he simply indicated that he thought the fixed levels were lower than the level would have been in fresh tissue.

Having regard to what his studies reveal concerning the effect of Klotz or Ely preservative solution (that is that the concentration of digoxin in the tissue decayed over time and there is a marked reduction) in my submission that is a reasonable suggestion by Mr. Cimbura. The question is simply we don't know how much higher they were.

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Will you turn then to Kristin Inwood, sir. In her case, sir, ante mortem and post mortem blood specimens are available, as are concentrations in fixed and exhumed tissues.

We can deal first, sir, with the ante mortem blood specimen. You will recall that -- from the Chart, sir, the ante mortem specimen that I am referring to was taken, the sample was taken on the 12th of March, 1981 and resulted in a reading at the Hospital of 2.6 nanograms. You will recall in this connection, sir, that Kristin Inwood suffered a medication error at 5:30 a.m. on the morning of March 12 when she inadvertently received a dose of digoxin intended for another patient. The incident report is Exhibit 113A. As a result of that error at 5:30 in the morning an ante mortem digoxin level was ordered and a level of 2.6 nanograms, well within the therapeutic range, is the level that was obtained later that day following the medication error incident.

There was, however, a further ante mortem sample taken on March 12, 1981 and tested at the Centre of Forensic Sciences. It disclosed no digoxin. That, sir, is the second sample referred to and tested.

THE COMMISSIONER: Yes. What time was



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2 it taken?

3 MS. CRONK: I was just coming to that,
4 sir. The difficulty is of the history of the specimen
5 is a little bit of a mystery. We know it was ante
6 mortem, because on Mr. Cimbura's report he has the
7 12th of March listed. That he has said is the date
8 on the specimen when he received it. We do not know,
9 however, on the circumstances under which it was
10 taken. It may very well be that it was a portion of
11 the specimen already tested at the Hospital on March
12 12th. I say, candidly, sir, that speculation, we
13 don't know if it was taken at a different time. The
14 only evidence available to us is that it was an ante
15 mortem specimen and that derives solely from the date
16 that appeared on Mr. Cimbura's report on the issue.

17 The only other blood specimen, sir,
18 is, of course, the one about which so much controversy
19 has arisen as the post mortem level resulting
20 in a reading of 491 nanograms. You will note, sir,
21 that it was received at the Centre of Forensic
22 Sciences on January 28, 1982. It was discovered,
23 you will remember, at the virology lab, and it had
24 been there at the Hospital for some nine or ten months.
25 It is clear from the evidence that we reviewed
yesterday that it was a serum specimen. You will



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2 recall my submissions to you, sir, that there is
3 no clear evidence that it was frozen before it was
4 assayed, although the suggestion has been raised
5 that there is clear evidence that it had been heated.

6 If we could then look at the fixed
7 tissues, sir, once again these were tested by use of
8 both the RIA and the HPLC procedure. The levels in the
9 left v ntricle and the septum of the heart are both
10 within the toxic ranges quoted by Mr. Cimbura.

11 In addition however, we have a
12 specimen of exhumed muscle tissue. That is Item No. 3
13 in the chart and a level of 166 nanograms was found.
14 The level in the exhumed muscle, again according to
15 Mr. Cimbura's report --

16 THE COMMISSIONER: I am sorry, I am
17 having trouble again. The toxic range for fixed
18 heart tissue I find where? It doesn't seem to be on
19 this.

20 MS. CRONK: I am sorry, sir, when I
21 refer to the ranges it is the only ranges that are
22 available. Mr. Cimbura, he has not provided a list
23 of toxic and therapeutic ranges particular to fixed
24 tissues.

25 THE COMMISSIONER: I see.

MS. CRONK: He has only been able to



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2 provide them in the context set out in the chart.

3 THE COMMISSIONER: Yes.

4 MS. CRONK: When I say they are in the
5 toxic range I am suggesting in this case that they
6 are fixed tissues. Generally, Mr. Cimbura's tests
7 have indicated that the levels in fixed tissues are
8 lower than they were in fresh.

8 THE COMMISSIONER: Yes.

9 MS. CRONK: I am referring to the
10 ranges that he has quoted for fresh tissue, not
11 fixed.

12 In this case, sir, he specifically
13 confirmed in his report and in his oral evidence here,
14 that those ranges in the left ventricle and the septum
15 are both within the toxic range. That evidence is
16 found at Volume 52, page 1659 to 1662.

17 The level in the exhumed muscle tissue
18 is within the toxic range, as well, according to Mr.
19 Cimbura. It was a level of 166 nanograms tested by
20 HPLC and RIA.

21 As a result, in the case of Kristin
22 Inwood, sir, we have measured concentrations in
23 post mortem blood, fixed heart tissue and exhumed
24 tissue, all within the toxic range, but we do not
25 have the measurements in fresh tissue.



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2 Once again, Mr. Cimbura was unable
3 to estimate a precise measurement or number in fresh
4 tissue, but suggested that the levels in the fixed
5 tissue were lower than the ones that would have been
6 found in the fresh tissue.

7 If we could turn then to Michelle
8 Manojlovich, the next case. The only levels available
9 on this child were ante mortem blood specimens and,
10 with respect to one of those, there is a side issue,
11 if I could express it that way. Her level on March
12 11, 1981, which was the day before her death, she
13 died, later that night, was 2.2 nanograms. That was
14 tested at the Hospital for Sick Children, using RIA
15 only. There was, however, a sample that was sent to
16 Hospital -- I am sorry, to the Centre for Forensic
17 Sciences, as well. It is reported in Exhibit 95A of
18 Mr. Cimbura's reports. He has indicated that he tested
19 it by RIA and HPLC and RIA and that he was unable to
20 obtain a measurement of pure digoxin, using the HPLC
21 and the RIA.

22 What we do not know, sir, is whether
23 or not this specimen was an ante mortem blood specimen
24 or a post mortem specimen. The only evidence, with
25 respect to that specimen in part flows from Dr. Rowe,
who has indicated that he is unaware of any post



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1 mortem blood specimens having been taken on Michelle
2 Manojlovich and from Mr. Cimbura who indicated that
3 he didn't, in fact, know whether it was ante mortem
4 or post mortem specimen. These are the only levels
5 available on this child at all. There are no tissue
6 specimens.

7 We come then, sir, to the case of
8 Kevin Pacsai. There are, in this case, as is apparent
9 from the chart, a number of levels measured in a
10 variety of specimens, including both ante mortem and
11 post mortem blood and, as well, in fixed and frozen
12 tissues.

13 Once again what we are missing are
14 levels in fresh tissues.

15 If I could deal, first, sir, with the
16 ante mortem blood specimen, because a number of issues
17 have arisen in the evidence with respect to this
18 level.

19 The ante mortem blood reading from
20 the Hospital for Sick Children was greater than 10
21 nanograms. It was tested by RIA. The evidence has
22 been that it was a sample taken by Dr. Costigan while
23 the child was in the Intensive Care Unit at
24 approximately 6 in the morning, 6:15, 6:30 on March
25 12th. The child, you will remember, died approximately



1
2 four hours later in the Intensive Care Unit.

3 This particular sample, sir, was sent
4 to the hematology lab where it was hemolyzed.

5 Dr. Costigan later found it there,
6 retrieved it and brought it personally to the bio-
7 chemistry lab for digoxin assay. That has been the
8 evidence of both Drs. Costigan and Ellis. When the
9 sample arrived in the biochemistry laboratory only
10 one tube of serum was available. It was, therefore,
11 divided into two parts and assayed. The first two
12 were assayed without dilution. You will recall, sir,
13 that Dr. Ellis spoke about assaying something neat.
14 His expression was neat without dilution. On that
15 without dilution reading -- sorry, assayed, the reading
16 was 5 nanograms. A computer projection of the actual
17 level, however, was recorded as 16 nanograms. Dr.
18 Ellis has testified that the computer projection in
19 this regard is unreliable.

20 MR. SHINEHOFT: I am sorry to interrupt
21 my friend, but I thought the level it showed was
22 greater than 10.

23 MS. CRONK: I am on the neat assay at
24 the moment, Mr. Shinehoft. It was then, as Mr.
25 Shinehoft points out, quite correctly, assayed again,
this time on a dilution of two, but the reading was



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2 greater than 10 nanograms. No further sample was
3 available, as you know for testing for further
4 dilution, sir, but the other point with respect to
5 that dilution times two, is that Dr. Ellis has
6 testified that the computer projection on that run,
7 on a dilution of 2, was either 5.3 or 10.6. He is
8 not sure which. That evidence, sir, is found at
9 Volume 49, page 1115 to 1116 and at page 1259 to
10 1260.

11 In light of that history, sir, two
12 questions arise with respect to the integrity of the
13 sample itself, and a third issue arises, or a third
14 question arises, as to what the likely ante mortem
15 level, in fact, was.

16 The two issues with respect to the
17 integrity of the sample, sir, are as follows: Is
18 there a problem in terms of the timing of the sample,
19 when it was taken and, secondly, what effect, if any,
20 did the hemolysis in the hematology laboratory have
21 on the digoxin concentration in the specimen.

22 I hope to assist you, sir, you may
23 recall a hemolyzed sample is one containing hemoglobin
24 from red cells due, according to some experts, from
25 red cell breakdown. The evidence has been there was
a concern that that implication or that that feature



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2 could cause distortion of the concentration of digoxin
3 in the blood specimen.

4 If I could deal with the time of the
5 sample first, sir. As I mentioned, Dr. Costigan
6 has given direct evidence before you that the sample
7 was taken by him between 6 o'clock in the morning and
8 6:30 in the Intensive Care Unit. The child died at
9 10:10 in the morning, again in the Intensive Care
10 Unit. He received his last known dose of digoxin at
11 9 o'clock the night before, the night of March 11th
12 and accordingly, in relation to the last known dose
13 a sample was taken a minimum of nine hours after
14 administration.

15 Dr. Ellis has testified that when he
16 learned of that timing he ruled out any possibility
17 that the sample had been taken prematurely, at least
18 in terms of the last known dose, although the Hospital
19 had been very concerned about that when they originally
20 got the ante mortem level back. The obvious, sir,
21 is true, we don't know if one posits an unauthorized
22 administration, we don't know at what time that might
23 have been.

24 The other implication of dose at
25 9 o'clock, sir, however, is the issue of whether or
not the amount that was, in fact given at 9 o'clock,



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was large enough, by inadvertence, or with deliberation so as to have caused the level seen in this child. We have heard evidence from a number of witnesses, including Nurse Nelles, Dr. Fowler, Mary Costello, Elizabeth Radojewski, that the amount that was given at 9 o'clock on the evening of March 11th was investigated and that the conclusion was, certainly by Dr. Fowler was that the prescribed dose had been given at 9 o'clock.

Nurse Nelles has testified that she, in fact, drew the drug up at that time in a tuberculine syringe and she remembers it was a tuberculine syringe because the plunger was out and that she double-checked the dose with Mary Jean Halpenny. You will recall that Miss Costello's notes of a meeting held on March 23rd record that Miss Nelles had said that at the meeting and that Mary Jean Halpenny, who was present, was recorded by Miss Costello as having confirmed that she, in fact, checked the dose.

It is my submission, therefore, on the evidence before you, it would appear that the dose, according to Dr. Fowler, was a proper one, as prescribed, and that it had been double-checked, as was required by the rules that applied to the cardiac wards at



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2 the time.

3 The second issue, however, relates to
4 the possible effect of this hemolysis of the sample.
5 Dr. Ellis has told us that a chemical called EDTA,
6 that is ethylenediaminetetracetic acid, sir, which is
7 used as a preservative for hematology samples,
8 EDTA.

9 The issue was raised as to whether or
10 not EDTA would cause a false elevation, a false
11 positive reading in a concentration of digoxin.
12 Dr. Costigan was concerned about this, as well, when
13 he realized where the sample was, where he found it.
14 To check against that possibility Dr. Ellis ran a
15 series of tests on March 17, 1981 on hemolyzed blood
16 specimen. His opinion, he has told you, sir, before
17 running those tests, was that it was unlikely that
18 EDTA would have interfered with the RIA assay at his
19 laboratory. His conclusion when the tests had been
20 done was that it did not.

21 We come then, sir, to the issue of the
22 significance of the computer projections and whether
23 or not they can help us in determining what, in fact,
24 the ante mortem Pacsai level was. Dr. Ellis, you
25 will recall, has testified that the computer projection
on the second assay, the dilution times 2 may, in fact,



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2 have been 5.3 or it may have been 10.6. If it was
3 10.6 he has testified that it is likely to be less
4 in error than the projection on the first run of the
12 assay, which was 16. His explanation for that opinion
5 was that the closer the measurement is to the
6 maximum that is detectable by the assay a greater
7 degree of reliance that he as a scientist can place
8 in it.

9 THE COMMISSIONER: I know we went
10 through this before. How could it be 5.3? How could
11 the computer result be 5.3 if the reading is greater
12 than 10?

13 MS. CRONK: That particular dilution,
14 sir, and that is why I placed some emphasis on it was
15 a dilution times 2. What that meant was, you will
16 recall the way the dilutions work at the Hospital for
Sick Children --

17 THE COMMISSIONER: Yes.

18 MS. CRONK: The projections could
19 actually have been 5.3. If that were the case on a
20 dilution of 2 you would multiply 2 times 5.3 to
21 produce a projection of 10.6.
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F-1

DM/hr

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THE COMMISSIONER: If it were 10.6.

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MS. CRONK: You would multiply it by
2 with a reading potentially of 21 plus.

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THE COMMISSIONER: I see.

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MS. CRONK: That is the difficulty,
sir. In the digoxin book itself the handwritten number
is 10.6. What Dr. Ellis has said is that he does not know
if that is the result of the multiplication that one
of the technicians did, or if in fact that was the
projected number.

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THE COMMISSIONER: Yes.

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MS. CRONK: As interesting as the
debate may be, Mr. Commissioner, as to whether or not
these computer projections can be relied upon as an
accurate reflection of what that ante mortem level was
we are in my submission not greatly advanced by the
exercise. The most that can be said on the evidence
before you is that the reading ante mortem may in fact
have been 10.6 nanograms as projected by the computer
or close thereto, or it may in fact have been 21.2
nanograms, we don't know and we can't find out
although what we do know is that the actual reliable
reading, reliable in the sense that is what was
reported was greater than 10 nanograms.

23

We come then to the post mortem blood

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F-2

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2 levels on Kevin Pacsai, Mr. Commissioner. I mentioned
3 a few moments ago that the evidence establishes that
4 that sample was drawn by Dr. Cutz at autopsy. You will
5 recall Mr. Lamek mentioning in opening two days ago
6 that Pacsai was the case where Dr. Cutz for the very
7 first time and of his own motion determined when he
8 had seen the Pacsai chart to take a blood sample for
9 digoxin assay although he had never done so before
10 on a post mortem basis. He did so he has testified
11 because of the indications of concern regarding
12 digoxin toxicity that were recorded by Dr. Costigan
13 in the medical chart of the child which he examined
14 at the commencement of the autopsy. The sample that
15 he did take sir, was tested at three different
16 laboratories. It was tested first at the Hospital
17 for Sick Children where it was assayed several times
18 on two different days. The results of each separate
19 set of assays confirmed a reading of 26 nanograms
20 per millilitre. Dr. Ellis has testified that after
21 the first set of dilutions, the first set of assays
22 were complete and he saw the reading, he was
23 concerned to cross-check it to make sure it was right
24 and he ran the assays again the next day and got
25 exactly the same reading, 26.

Dr. Ellis has further testified that he



F-3

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2 personally checked the assay results on both days
3 to satisfy himself that they had been performed
4 correctly. He has said to you, sir, that he was
5 satisfied that they were and that he regarded the
6 level as valid.

7 The same specimen however, sir, was
8 tested as well at Mt. Sinai Hospital at the request
9 of Dr. Ellis. A different RIA antibody and separation
10 technique were used at that Hospital. The level
11 reported from the laboratory was 112 nanograms per
12 millilitre. Obviously, sir, apart from the discrepancy
13 in the numbers the item of interest is it was the
14 very same autopsy blood specimen. Dr. Ellis has
15 testified that he attributes the discrepancy in the
16 two numbers to the differences in the methodology
17 between the two antibody techniques. The burden of
18 the evidence if I can describe it that is before you,
19 sir, by the various pharmacologists who have attempted
20 to interpret this number along with all the other
21 numbers in Kevin Pacsai's case is that the number is
22 inconsistent quantitatively with the numbers from
23 two other laboratories, that is the Hospital for
24 Sick Children and the Centre of Forensic Sciences,
25 so they would not place any reliance on it quantitatively.
It is however, corroborative that there was a very high



F-4

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2 reading in Kevin Pacsai's post mortem blood.

3 Finally at the Centre of Forensic
4 Sciences the third laboratory where it was tested,
5 sir, this was tested there for the very first time
6 using a full HPLC extraction and RIA process, the
7 results confirm exactly the level reported by the
8 Hospital for Sick Children, that is 26 nanograms.

9 THE COMMISSIONER: That is the same
10 sample?

11 MS. CRONK: The same sample, sir.
12 So we are in this situation. In my submission, sir,
13 we have a reading on RIA only at the Hosptial for
14 Sick Children of 26, that reading has been confirmed
15 by use of the HPLC extraction and RIA technique on
16 the same sample a reading of 26 and we have this
17 anomalous result of 112. The post mortem level itself
18 is clearly within the range of toxic values established
19 by the literature, although at the lower end. Several
20 witnesses have testified before you, sir, that this
21 post mortem level in fact served to confirm in
22 their minds the ante mortem level that they felt the
23 results to be consistent.

24 We come then to the tissueresults on
25 Kevin Pacsai. As I mentioned a few moments ago, sir,
we are confined in this case to fixed and frozen



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tissues. If we can deal with those on part first. You will note, sir, they were measured by RIA and HPLC and RIA with the exception of the left atrium, they are slightly below the toxic range reported for fresh tissues but Mr. Cimbura estimated that the values would be higher in the fresh tissue than in the fixed. When I say they are slightly below the toxic range, sir, I am referring only to the two that were measured by HPLC.

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Then we come to the lung tissues, sir, and you will see that there were two specimens, one fixed and one frozen. Both were assayed by Mr. Cimbura using the HPLC and RIA techniques. The level in the fixed specimen was 48 nanograms per gram and is well within the toxic range and well above the therapeutic range reported by Mr. Cimbura. The level of the frozen specimen is again well above the therapeutic range and was so expressly reported by Mr. Cimbura. In consequence then we have post mortem and ante mortem blood specimens and lung tissue readings well in the toxic range as reported, with heart tissue when fresh likely in the toxic range as well. I make the latter statement, sir, having regard to the numbers that were recorded in the fixed heart specimens from Pacsai, the 105 nanograms in the left ventricle



F-6

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2 on HPLC and 102 in the septum on fixed. Mr. Cimbura
3 has expressed the opinion that those levels are likely
4 lower than those that would have been found in fresh,
5 but we know from his ranges for fresh that the toxic
6 range starts at 108, so it is likely that the fresh
7 tissues had a concentration as well within the toxic
8 range but the overlap range.

9 THE COMMISSIONER: Yes, all right. Would
10 you like to take 20 minutes now?

11 MS. CRONK: That would be fine.

12 --- Short Recess.

13 --- On resuming

14 MS. CRONK: Thank you, sir. Sir, there
15 are two matters to which I would like to briefly
16 return. The first concerns the list of 12 children
17 that I outlined earlier this morning. You will recall,
18 sir, that my observation with respect to those 12
19 was as follows: that in respect to those 12 children
20 Mr. Cimbura reported levels of digoxin within the
21 toxic or fatal range. I do not wish, sir, for it to
22 be taken from that statement that he concluded in
23 any way that any or all of those 12 children died
24 from digoxin toxicity. My observation was directed
25 to simply what the ranges of levels meant that he
had reported.



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THE COMMISSIONER: I take it it is
in the toxic and not in the therapeutic.

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MS. CRONK: That is correct, sir.
As you know, Mr. Lamek will be dealing in detail with
the analysis of the cases of all 36 of the children,
including those 12, and the opinions offered by various
experts as to whether or not digoxin did in probability
contribute to their death.

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The second point to which I would like
to return, sir --

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THE COMMISSIONER: Yes, Mr. Tobias.

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MR. TOBIAS: I apologize to Miss Cronk
for interrupting her. I was advised my client was
one of those 12 that you referred to. Do I understand
your comment to the Commissioner, the last comment
that you made, that the reportings of Mr. Cimbura
were that the levels were in the toxic and yet not in
the therapeutic range? Because with respect to Hines
I think in fairness it has been my understanding that
the levels were in the overlap range, they fell into
both.

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MS. CRONK: You may be right. I was
referring primarily to the lung specimen, because the
liver specimen on Hines was not tested by use of HPLC
and I will confirm that in just a moment.



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2 THE COMMISSIONER: I take it
3 all you needed for that statement was one
4 finding.

5 MS. CRONK: That is correct, sir.
6 I am sorry, sir, Mr. Tobias is quite correct, the
7 fixed lung reading, and we will come to this in due
8 course, was within both the therapeutic and the toxic
9 ranges. My remark was it was in the toxic range as
10 well, it is within the overlap area.

11 THE COMMISSIONER: And so "not in the
12 therapeutic" is wrong I take it for all of the 12?

13 MS. CRONK: I will double check that
14 whole list in light of that, that had been my
15 intent but obviously an error was made with respect
16 to Hines and I will check that and let you know, sir.
17 I am grateful to my friend, thank you.

18 MR. TOBIAS: Thank you.

19 MS. CRONK: There is another area
20 sir, to which I would like to return, that concerns
21 the ante mortem blood specimen on Kevin Pacsai. You
22 will recall, sir, that one of the issues raised with
23 respect to the integrity of that sample, or whether or
24 not EDTA could have contributed to a false elevation
25 in the concentration of digoxin in tests run by Dr.
Ellis. In his opinion it demonstrated that it was



F-9

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2 not likely to and in fact did not. I am told by
3 some of my friends that I may have suggested as well
4 that the sample was thought to have been hemolyzed
5 If I did make that suggestion, sir, I did not intend
6 to. The evidence is that the sample was contained
7 in an EDTA tube, a hematology laboratory tube and the
8 thought was that there might be some of that chemical
9 present and that was the issue with respect to the
10 integrity that was raised.

11 THE COMMISSIONER: Yes, all right.

12 MS. CRONK: We turn then, sir, to the
13 case of Barbara Gionas and she is at page 7 of the
14 charts that have been marked, sir. You will see that
15 there are three ante mortem blood readings available
16 on Barbara Gionas, all well within the therapeutic
17 range that we discussed yesterday, that is between
18 the range of 1 and 3 or 3.5, no post mortem blood
19 levels are available. The only tissue specimens
20 available from this child, sir, are exhumed tissues.
21 In addition the baby's body had been embalmed. All
22 the tissue tests you will see going right down the
23 list that six different types of tissues were tested,
24 all were tested using the HPLC and RIA technique.
25 The levels reported in heart and muscle tissue are
within the range reported for fresh tissues after



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digoxin therapy, that is they are in the therapeutic range. In the case of heart they are as well in the overlap area and they are also in the toxic range. The levels for both the liver and the lung tissues are in the toxic or fatal ranges.

THE COMMISSIONER: The liver and which, did you say the lungs?

MS. CRONK: In the lungs, sir. You will see that both the specimens of the right and left lung were tested, the results were .225 nanograms and 205 nanograms respectively. The overlap area, for lung tissue as quoted by Mr. Cimbura ends at 30 and both of them are therefore not in the overlap area but rather are clearly within the toxic area for fresh tissue specimens; and the same sir, applies to the liver tissue of 207 nanograms beyond the overlap and into the toxic range.

THE COMMISSIONER: All right, thank you.

MS. CRONK: When we come to Jordan Hines as Mr. Tobias has already quite appropriately pointed out, sir, there were a number of tissue specimens tested. This is a case, sir, where clearly we have no ante mortem blood specimens at all because the child had not been on prescribed digoxin therapy.



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There are no post mortem blood levels available. We have fixed tissue levels and exhumed tissue levels, no fresh tissues.

THE COMMISSIONER: The liver tissue that is exhumed.

MS. CRONK: That is exhumed, sir. So we have fixed and exhumed tissues but no fresh tissues.

THE COMMISSIONER: Yes.

MS. CRONK: Dealing first with the fixed heart concentration, sir, you will see that these tests were conducted, with one exception, using the HPLC/RIA technique. With respect to the two specimens tested using HPLC the levels were in the therapeutic range as measured by Mr. Cimbura. He, however, estimated that the concentration of digoxin in the fresh heart would likely be 252 nanograms per gram, that range, that measurement, if it be so, if that was what was within the fresh heart is within both the therapeutic and the toxic ranges, it is in the overlap area.

THE COMMISSIONER: I am sorry, from the heart tissue?

MS. CRONK: Yes, sir. I am referring now to the left ventricle reading and the septum reading which are the only two of the three that were done



F-12

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on HPLC and RIA.

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THE COMMISSIONER: Heart tissue, I
don't have any heart tissue, I am looking at the chart.

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MS. CRONK: Sorry, sir, in the ranges.

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THE COMMISSIONER: Yes.

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MS. CRONK: The heart tissue is set
out as heart muscle.

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THE COMMISSIONER: Oh, I see, yes.

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MS. CRONK: Ranges B and you will see,
sir there is a very broad overlap area for heart
muscle, so that the levels of 52 nanograms and 89
nanograms that were the actual measurement on the
fixed tissues are well within the therapeutic range.

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THE COMMISSIONER: Yes, all right.

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MS. CRONK: The point of significance
in my submission, sir, is that Mr. Cimbura was in this
case able to do not only an estimate as to whether the
levels would be higher in fresh tissue but as to
the precise amount that he felt may well have been
present, he estimated that to be 252 nanograms and if
that be so it is clearly within both toxic and the
therapeutic ranges.



G-1

EMT/ac

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THE COMMISSIONER: Which one does
he estimate to be the 200?

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MS. CRONK: The heart itself, sir,
fresh heart tissue before it was placed in preservative
solution.

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THE COMMISSIONER: Yes.

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MS. CRONK: - he estimates to be
252 nanograms.

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THE COMMISSIONER: Yes. All right.

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MS. CRONK: You will have to -

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THE COMMISSIONER: Are we talking
about the septum, ventricle or -

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MS. CRONK: He did not distinguish,
sir.

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MR. TOBIAS: Page 6, Exhibit 95A
is where it is.

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MS. CRONK: It is actually page 7,
sir, note no. 1. Concentration of digoxin in the
heart before it was fixed in the Klotz solution was
estimated to be not less than 252 nanograms. So in
Mr. Cimbura's opinion the heart tissue before it was
fixed would have had at least 252 nanograms. And
if that be the case it is clearly within both the
therapeutic and toxic ranges as he set them out,
sir.



G-2

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2 You recall that I mentioned, sir,
3 that in some instances he was unable to arrive at
4 a precise measurement as to the expected or anticipated
5 concentration in fresh tissue. Hines is a case
6 where he was able to do so, and he expressed it as
7 a minimum; not less than 252.

8 THE COMMISSIONER: Yes. All right,
9 thank you.

10 MS. CRONK: If we could look then
11 at the fixed lung tissue in the case of Jordan Hines,
12 sir, again this was measured using the HPLC method,
13 and the level was within the overlap area. That is
14 both within the therapeutic and the toxic ranges.

15 The exhumed liver specimen was well
16 above the therapeutic level, but it was tested by
17 RIA only; not by HPLC.

18 Once again, sir, a statement of the
19 obvious: the fact that measurements were achieved
20 using HPLC of what Mr. Cimbura believed to be pure
21 digoxin in a child for whom a drug had never been
22 prescribed is qualitatively significant of and in
23 itself.

24 Can we turn then, sir, to the case
25 of Colleen Warner? Once again, sir, there are no
blood levels here, be they ante mortem or post mortem



G-3

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2 to assist us. The only levels available are on
3 fixed tissues from the heart.

4 All of those tissue specimens were
5 tested using the HPLC extraction method. The levels
6 in the left ventricle were in the toxic range while
7 the levels in the left atrium and the septum were
8 in the therapeutic range. If we look specifically
9 at the left ventricle, 119, you will see, sir, that
10 it is within the overlap area. It falls both within
11 the therapeutic and toxic range, whereas the other
12 two are well within the therapeutic.

13 Mr. Cimbura in this case, however,
14 arrived at an estimate as to the minimum concentration
15 he felt would have been present in the fresh heart
16 tissue. He expressed that to be not less than 284
17 nanograms per gram. Once again if that be so, the
18 concentration would be clearly in both the therapeutic
19 and the toxic ranges; the overlap area.

20 We go next then, sir, to the case of
21 Jennifer Thomas who died on February 12th, 1981.
22 Again there are no ante mortem or post mortem blood
23 specimens to assist us. There are, however, fixed
24 tissue specimens and only fixed tissue specimens.

25 In this case, however, we have them
from both the heart and the lung. The levels measured



G-4

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2 in the fixed heart specimens using HPLC were measured
3 on the left ventricle and the septum. They were
4 within the therapeutic range and not the toxic range.
5 Again for fresh tissue.

6 The level in the fixed lung was 45
7 nanograms. That was above the therapeutic range for
8 measurements in fresh lung and it is within the
9 toxic range. Outside the overlap and in the toxic
10 range. And as I note, sir -

11 THE COMMISSIONER: I'm sorry, let
12 me get this. The lung? Oh, yes.

13 MS. CRONK: The fixed lung tissue.
14 And I note, sir, with respect to that specimen that
15 it was tested by HPLC and RIA.

16 And finally Mr. Cimbura again was
17 unable to estimate a minimum amount of concentration
18 that would have been present in fresh tissue, but
19 repeated his view that the levels in both the heart
20 and the lung when fresh would have been higher.

21 We come then to the case of Bruce
22 Floryn, Mr. Commissioner. We have only one ante
23 mortem blood level taken within two weeks of the
24 child's death. It was taken on January 22nd. The
25 child died on February 7th, so it was some considerable
period of time before the date of death.



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The level was 2.1 nanograms; well within the therapeutic range under anyone's definition. When we come to examine the tissues we have in this case fixed and frozen tissues. The fixed tissues are from the heart; the frozen tissue is as well from the heart, a sample of heart muscle.

The fixed measurements were all well within the therapeutic range. None were tested, however, by HPLC, and the implication of that, sir, is that even on the highest reading available, and by that I mean the most uncertain in the sense that they may well have included digoxin-like substances or cross-reactants with the antibody, even under those circumstances the levels were well within the therapeutic range.

When we come to the frozen specimen, however, it was tested by use of the HPLC method. A level of 60 nanograms was recorded. That is well within the therapeutic range for fresh tissue and well below the fatal range, sir. As again quoted by Mr. Cimbura.

We come next then, sir, to the case of Janice Estrella and of course there is an area of interpretative difficulty specific to this child's specimens, particularly her post mortem blood specimens.



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If we could deal with her tissue readings first, sir, and then return to the blood specimens, the only tissue specimens available for testing were fixed specimens from the heart. They were all tested using the HPLC and RIA technique and the result after HPLC was 4 nanograms per gram.

Mr. Cimbura has explained that the expression of that measurement was in fact a composite of all the tissues measured. He estimated that the concentration of digoxin in the fresh heart was not less than 55 nanograms per gram. If that be so, sir, the concentration in the heart, if 55 of thereabouts, is well within the therapeutic range. It would have to be higher than 108 to move into the overlap area. Again that was expressed as a minimum by Mr. Cimbura.

THE COMMISSIONER: Why in your chart, so that I will understand, is the heart muscle - why have we used the term heart muscle up in B? In many of the instances it seems to me it applies to any part of the heart, doesn't it?

MS. CRONK: Yes, you are quite right, it does, sir, and as I recall it, if we could take a look at Exhibit 95A, page 4, note 3, Mr. Cimbura in that particular instance is talking about ventricular muscle of infants and he quoted the



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therapeutic range as 49 to 975. And he reports the concentrations in cases of fatal poisoning as being 108 to 1240.

THE COMMISSIONER: Yes. Well, what is concerning me, I don't quite understand because there must have been -

MS. CRONK: You have to read that range, sir, with the items under no. E at the bottom of the chart, fresh autopsy specimens.

THE COMMISSIONER: Yes.

MS. CRONK: You will see that he had a case of the left ventricle, the heart, where there was a reading of 1252. You will see that he had a reading in the left atrium of the heart of -

THE COMMISSIONER: Where are we looking?

MS. CRONK: I'm sorry, sir.

THE COMMISSIONER: Yes. All right.

MS. CRONK: - of 631. I'm sorry, sir, I think we are on the wrong document. The chart that I provided to you sets out various ranges.

THE COMMISSIONER: Yes.

MS. CRONK: Heart muscle is under item B; fresh autopsy specimens are under E.

THE COMMISSIONER: Yes.



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MS. CRONK: You will see, sir, he has reported levels in particular areas of the heart. In addition to ventricular muscle he has included left ventricle where there was a case of 1252 nanograms per gram.

THE COMMISSIONER: I understand all that, but do we not have for these portions of the heart, we do not have any therapeutic range?

MS. CRONK: The therapeutic and the toxic ranges as advanced by Mr. Cimbura as set out under B, sir, are a composite of the ranges reported under E.

THE COMMISSIONER: Oh, I see, a composite of?

MS. CRONK: Of the heart levels under E.

THE COMMISSIONER: Yes. A composite of all under E.

MS. CRONK: As he explained it, sir, the way the evidence came forward he originally expressed the therapeutic and toxic ranges for heart in terms of the heart muscle. That was in his oral testimony here.

If you look at his actual references in his reports he is talking about ventricular muscle



G-9

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2 from the heart, but he then related that as well to
3 cases that dealt with the left atrium and to the
4 heart generally and suggested it was really an
5 expression of what he felt to be a reasonable range
6 for specimens from those particular areas in the
7 heart as well. I agree it is not as clear as it
8 might be.

9 THE COMMISSIONER: On the heart
10 muscle we have a fatal range of 108 to 1240. If you
11 look at the fresh autopsy specimens you have the
12 heart, I don't know, 100 and 200, and then you have
13 the left ventricle at 1252 in one case and left
14 atrium 631. Those things I find very hard to under-
15 stand.

16 MS. CRONK: Well, sir, the left atrium,
17 for example, 631, would clearly be within the overlap
18 area that he has described for heart muscle. It is
19 clearly within the therapeutic range and it is clearly
20 within the toxic range.

21 THE COMMISSIONER: I understand all
22 of that, but I don't quite understand why in your
23 chart we have fresh specimens, we have the heart
24 muscle and you now tell me that is really heart tissue.
25 That is anything, any part of the heart, is that
right?



G-10

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MS. CRONK: As I understand -

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THE COMMISSIONER: B is any part

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of the heart?

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MS. CRONK: As I understand Mr.

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Cimbura's evidence that is what he intended the range
to represent.

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THE COMMISSIONER: All right. Then

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why do we need to have the fresh autopsy specimens

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for the heart as well? Then we also have the lung

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and the liver - the lung and the liver which we also

11

have up above.

12

MS. CRONK: Sir, they were included

13

on the chart in an effort to be complete. The fact

14

is that in Mr. Cimbura's reports he expressed the

15

first four types of ranges in various parts of his

16

reports but in a later report he then as well set out

17

levels based on particular case reports that he had
read, and that is item E.

18

THE COMMISSIONER: I see. That is

19

from 95A, I take it?

20

MS. CRONK: That is correct, sir,

21

on page 2.

22

THE COMMISSIONER: All right. Well

23

then I will blame him and I won't blame you.

24

MS. CRONK: I am prepared well to

25



G-11

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shoulder some of it, sir.

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THE COMMISSIONER: No, no, no.

4

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MS. CRONK: And I agree it is not
as clear as it might have been.

6

Could we look then, sir, further
at the case of Janice Estrella?

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THE COMMISSIONER: All right.

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MS. CRONK: Dealing with her ante
mortem blood specimens, as you know, sir, Janice
Estrella's ante mortem blood readings were considered
at one stage in the toxic range. On January 7th she
had a reading of greater than 9.4. It was on that
day that her digoxin was held, and it was not restarted
prior to her death. On January 8th the level had
fallen to 7.8, still significantly above the therapeutic
range under any definition that has been advanced for
infants. On January 9th it fell to 4.7. That was
the last ante mortem level reading available.
Controversy surrounds obviously the two post mortem
specimens.

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Dr. Taylor you will remember was the
pathology resident who conducted the autopsy on
Janice Estrella. Of interest it was conducted some
11½ hours after her death on January 11th. He has
testified specifically as to the way in which he went



G-12

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about taking both of those specimens.

He has told us that he personally took a sample both from the femoral leg vein and from the pelvic cavity. I would like to deal, sir, specifically with the issues that have been raised on the leg vein sample and in more particularity with the sampling technique that was used. He has testified that the body - that by the time he remembered to take a specimen and went back, the body had in fact been stitched up and taken to the morgue.

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I.1.1.

RD/ac

1 When he went to take
2 his specimen he went with a colleague. The body
3 was re-opened and unstitched and his colleague elevated
4 the legs and milked the veins by using one hand to
5 hold the leg up and using the other hand to squeeze
6 the calf muscle and the thigh muscle to try to force
 blood from the deeper leg veins out.

7 Dr. Taylor has said that he allowed
8 a little bit of blood to drain from the vein and
9 then applied the tip of a syringe to the area of the
10 opening of the vein and pulled back on the plunger
11 to allow blood to enter. He did not use a needle.
12 The sample that he took was, in fact, a mixture of
13 a small amount of blood from both legs, not just from
 one.

14 He testified, however, sir, that he
15 took certain precautions to minimize the risk of any
16 contamination of that sample. Specifically he felt
17 that by refraining from using a needle he had
18 minimized the chance that any fragment of tissue might
19 have attached to the needle and thus entered the blood
20 sample. Secondly, he cleaned and dried the tissues
21 surrounding the sample site before taking the
22 sample. Third, he felt that allowing a few drops of
23 blood to flow out before he used the syringe to take
24 the sample ensured that any adjacent tissue fragments
25



H.1.2.

1
2 would not have entered the sample and, finally,
3 he specifically chose the leg vein site in preference,
4 initially to any other site, because he thought
5 that the leg vein site was the only one available
6 from which he could obtain a clean specimen. In
7 other words, we know he took two. He took one
8 first from the leg vein for that very reason, because
9 he thought it was the only site available under
10 the circumstances, which would permit the obtaining
11 of a clean sample.

12 He expressed the opinion, sir, in
13 light of those precautions that although there was
14 a possibility that the leg vein sample could have
15 been contaminated he thought it was a clean sample,
16 contaminated, if at all, to an insignificant degree.
17 His evidence is found, sir, at Volume 43, page 8887
18 and page 8630 to 8632.

19 When we come to the pelvic cavity
20 sample -- much has been said about this already,
21 sir, and I won't deal with it in detail, but
22 Dr. Taylor recognized in his evidence that there was
23 a risk of contamination from a number of factors on
24 this sample; first by tissue fluids; secondly from
25 the the acetic fluid the child had; third from the
water that had been used to wash the body down upon



H.1.3.

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2 completion of the autopsy and; fourth, the potential
3 was that it could have been contaminated from
4 fecal material or urine inasmuch as the bowel had
5 been cut during the autopsy.

6 He testified that in his opinion
7 it was probable that there was some edema fluid in
8 the cavity at the time that he took the sample,
9 although he didn't know whether or not the edema
10 fluid contained digoxin.

11 He also testified it was probable
12 that acetic fluid in the cavity was present, although
13 most of it he thought would have been drained off
14 by the time of completion of the autopsy and, once
15 again, he didn't know whether that fluid contained
16 digoxin. He expressed the view, sir, that those
17 two agents were the largest possible contaminants
18 of the sample, that is the edema fluid or the acetic
19 fluid, although it was also possible that the other
20 factors could have contributed.

21 You will recall, sir, as well, that
22 in Janice Estrella's final autopsy report found in
23 her medical chart, it was signed by both Drs. Taylor
24 and Mancer, contamination of the sample by only
25 those two factors was mentioned, that is edema and
acetic fluid and it was described as slight.



H.1.4.

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We have heard from a large number of experts, Mr. Commissioner, as to the likelihood that either or both of those two post mortem samples were contaminated. In my submission, in light of the evidence of Dr. Taylor, which I suggest is the best evidence under the circumstances, as to how the sample was, in fact, obtained, the real risk of contamination obviously flows from the pelvic cavity sample, and is not a substantial risk with respect to the leg vein sample at all.

Again, sir, the significance if any, to be attached to the pelvic cavity reading will fall, according to the significance attached to the gutter blood study results.

If we could look then, sir, at the case of Jesse Belanger, which falls into a somewhat different category than the other children.

The only measurements available in this case are from exhumed liver and muscle tissue. The exhumed muscle tissue was tested by HPLC and RIA plus the normal RIA procedure and a level of 43 nanograms resulted. In Mr. Cimbura's opinion that range was within the therapeutic range in fresh autopsy specimens of infants after digoxin therapy.



H.L.5.

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2 That level, therefore, was not of concern.

3 We then come to the exhumed liver
4 tissue, however, sir, and Mr. Cimbura has testified
5 that this is one of the three instances in which
6 he utilized the mass spectrometry technique as well
7 as his usual RIA and HPLC/RIA technique. He has
8 testified that a number of very specific assays
9 were done with respect to this specimen: first there
10 were two separate mass spectrometry tests done on
11 the specimen. The result of the first was negative
12 with a notation by the mass spectrometrists that
13 the extract was very impure. Mr. Cimbura, therefore,
14 attempted to purify more of the specimen, itself,
15 by subjecting it to successive HPLC purification
16 tests and then had another mass specs test done.
17 The reported result in that instance was that the
18 digoxin may be present but the extract was still
19 not ideal.

20 The mass spec results Mr. Cimbura
21 said in his opinion, were therefore inconclusive
22 of and by themselves.

23 In light of what he took to be the
24 inconclusive nature of the results he devised another
25 HPLC procedure using a different kind of column and
a different mode of liquid chromatography and after



H.1.6

1
2 he performed that on the specimen another RIA assay
3 was done. Mr. Cimbura also obtained and used a
4 different RIA antibody from a different manufacturer
5 and assayed the specimen using that kit. The
6 results, sir, were in this position in terms of the
7 actual steps that were used to test the specimen.
8 Mr. Cimbura's normal RIA and HPLC procedure was
9 used. Two different mass spec tests were done. A
10 separate HPLC and RIA test, using a different
11 procedure and column, were done and two different
12 RIA assays were done with two different RIA antibodies.
13 The results expressed by Mr. Cimbura are based on
14 a combination of all of those tests. His evidence
15 has been that in light of the multiplicity of the
16 tests and the different antibodies used and
17 the different columns used on the HPLC test that
18 he had a high degree of confidence that what he
19 had in fact measured was pure digoxin.

20 The level of 253 nanograms, sir,
21 he reported is above the therapeutic level reported
22 for fresh liver tissue. As you will see from the
23 chart, the cutoff there is 190 nanograms is well
24 above that and it is within the toxic range. It was
25 Mr. Cimbura's opinion that the result, itself, was
inconclusive with respect to digoxin toxicity although



H.1.7.

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2 it qualitatively confirmed both the presence of
3 digoxin and the fact that Jesse had received digoxin
4 when it hadn't been prescribed for him.

5 Specifically, with respect to
6 Belanger, Mr. Cimbura was again asked whether or not he
7 could with any reasonable degree of scientific
8 certainty say that the measurement that he had
9 achieved had excluded Substance X and his answer
10 was the same, sir, but enhanced in this
11 situation, given that there were really six or
12 seven different kinds of techniques applied to this
13 specimen, he was confident that he had, in fact,,
measured digoxin and not Substance X.

14 We are in much the same position
15 with Stephanie Lombardo, sir. Again no blood levels
16 are available, ante mortem or post mortem. All of
17 the levels are from exhumed tissues, just as they
18 were in the case of Jesse Belanger. This child,
19 however, had not been embalmed. The specimens from
20 Jesse Belanger -- I'm sorry, three specimens from
21 Stephanie Lombardo were tested using mass spectrometry
22 as well as HPLC and the normal RIA procedure. These
23 were the chest fluid and two samples of heart tissue,
24 as you will see from the chart. The results were
25 all reported by Mr. Cimbura as pure digoxin on the



H.1.8.

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2 basis of the number of tests that were done. He
3 regarded the MS results of Stephanie Lombardo's
4 tissues as a positive finding of digoxin, as it had
5 already been disclosed by the previously run HPLC
6 and RIA tests.

7 In addition, sir, a particular
8 note in Stephanie Lombardo's case, is that a great number
9 of other tissues were tested using the RIA and
10 HPLC methodology, the liver, the lung, the
11 muscle, the stomach and the small bowel. Substantial
12 amounts of digoxin were found using the HPLC method
13 in all of the tissues from Stephanie Lombardo. The
14 levels were, in fact, the highest recorded by
15 Mr. Cimbura from any exhumed tissues.

16 Mr. Cimbura moreover, regarded the
17 levels as conservative estimates of the concentrations
18 that would have been present in this child's fresh
19 tissues.

20 Drs. Spielberg, Mirkin and Kauffman
21 agreed that given the nature of the tests that had
22 been run on the chest fluid and the heart specimens
23 it was probable that Mr. Cimbura had, in fact,
24 measured pure digoxin.

25 There are, in my submission, sir,
several important distinguishing features concerning



H.1.9.

1
2 the Lombardo case from other cases. The first
3 is obviously that she is one of the four, for whom
4 digoxin had never been prescribed, but, secondly,
5 like Belanger mass spectrometry was used and in
6 the opinion, not only of Mr. Cimbura, but, as I said,
7 Drs. Spielberg, Mirkin, Kauffman and Hastreiter,
8 confirmed conclusively the presence of digoxin in
9 her heart tissues and chest fluid.

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The third feature is my submission, sir, is that it is significant that her tissues had not been placed in a preservative of any kind and that she had not been embalmed, so although there might be the risk as all the experts have said of degradation in the digoxin concentrations by virtue of the burial process and the lengthy period of time that it had been buried that risk is not presented by virtue of a fixative solution or an embalming fluid, so it is simply not fact.

In the fourth observation, sir, is that the vast number of tissues that were in fact tested here were all tested using HPLC. She had the highest levels of digoxin in any exhumed tissues, even though the body had been buried for some 18 months to two years before the assays were conducted. They were found in a great variety of tissues in significant amounts.

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H-2-2

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3 Mr. Cimbura was unable to approximate
4 an actual concentration that would have been found
5 in her fresh tissues, but again the general thesis
6 advanced by him is that the levels would have been
7 higher.

8 We turn then to the case of John
9 Onofre, sir. The only blood level available is an
10 ante mortem level taken some six days prior to his
11 death. It was well within the therapeutic range
12 of 1.1 nanograms. The only tissue specimens are again
13 exhumed specimens from the liver, the tongue and
14 the thigh and in addition this child was embalmed.
15 Mr. Cimbura reported that the measurement in the liver
16 and the muscle tissues, which had been done on HPLC
17 were within the therapeutic range. He did not indicate
18 whether or not this was so for the tongue tissue and
19 we have no ranges that have been provided to us for
20 tissue specimens of that type.

21 I should say, with respect to the
22 liver tissue, sir, that the reading of 163 is not
23 within an overlap area. It is only within the
24 therapeutic range and the same is true according to
25 Mr. Cimbura with respect to the thigh muscle.

THE COMMISSIONER: I am sorry, you say



H-2-3

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the liver?

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MS. CRONK: I am sorry, it is within the overlap area, I am sorry.

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We have no range expressed formally by Mr. Cimbura in his reports, but he has made a note to this particular case saying that it was within the therapeutic range.

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Then we come to the case of Matthew Lutes, sir. The only blood level available is one taken two days prior to death. Its reading was well within the therapeutic range at 2.1 nanograms. We are confined to fixed tissue readings in this case from the heart and from the lung. Most of the specimens were done using HPLC and RIA and on the left ventricle and the septum, which was the two areas of the heart tissue that were tested, using HPLC, no digoxin measurement was recorded. The level measured on the lung tissue was 5 nanograms per gram, which is within both the therapeutic range and the toxic range set out by Mr. Cimbura.

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We come then to Francis Volk, sir. There is very limited toxicological data available on this child. There is one ante mortem level obtained a month before the child died. It was 1.4 nanograms, again well within the therapeutic range. The only



H-2-4

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2 tissue specimen was a frozen specimen from skin. The
3 level reported was 28 nanograms. Mr. Cimbura reported
4 that was within the therapeutic range for skin tissue.

5 In the case of Brian Gage no post
6 mortem blood readings are available. His last ante
7 mortem reading and by last, closest in point of time
8 to death, was 3.5 nanograms. That was tested on the
9 actual day of his death and, of course, is at the
10 upper end of the therapeutic range and beyond it,
11 according to some witnesses. Two earlier readings in
12 mid August and mid September were both well within
the therapeutic range.

13 You will recall, sir, that a patient
14 incident report was filed with respect to this child
15 as well. It is Exhibit 308. It indicates that he
16 received two doses of digoxin on the morning of
17 September 24th instead of the one dose that it was
intended that he receive.

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2 A blood sample was therefore taken
3 seven hours after the accidental dose was given and it
4 was that blood sample that led to the reading of
5 3.5 nanograms. It is not unreasonable to conclude,
6 in my submission, that the slight elevation in the
7 level was therefore due to the double dosing that
8 morning.

9 The tissue levels tested from the child
10 were measured entirely from exhumed tissues. The
11 bowel specimens and the small intestine specimens were
12 tested using the HPLC method, as was fluid from the
13 bowel and the intestines. Mr. Cimbura indicated that
14 the levels did not appear to indicate digoxin toxicity
15 although the long burial and decomposition may have
16 affected the findings rendering the levels in his
17 opinion inconclusive one way or the other. A specimen
18 of exhumed thigh muscle was tested as well, sir, but
19 it was only on RIA and accordingly, in my submission,
20 lends itself to difficulties in extrapolating from
21 it.

22 In the case of Amber Dawson, sir, you
23 will recall she died on July the 28th, 1980. We have
24 only one ante mortem blood level available prior to
25 her death, dating from four days before the date of
her death, the level was 1.9 measured on RIA at the



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Hospital, again in the therapeutic range. The only tissue specimens available are from fixed tissues, sir, from the heart and from the lung. In those instances where they were subjected to HPLC no digoxin reading was recorded. Mr. Cimbura did however estimate that the fresh heart and the lung tissues would have contained digoxin when fresh but in an unknown amount, he was unable to say whether it would then have been in the therapeutic or the toxic range.

At first blush, Mr. Commissioner, the levels appear to negate digoxin toxicity. However, Mr. Cimbura has testified that her tissues were in Klotz solution for approximately 18 months before they were assayed. His studies demonstrated, and by this I am referring, sir, to the studies on Klotz solution and on tissues that were tested, demonstrated that considerable degradation of digoxin concentrations in fixed tissues can occur in as little as one to two months, certainly in six months, such that fixed tissues after that length of time might disclose no digoxin at all although high concentrations were present in the fresh tissues.

You will recall, sir, that those studies have been filed before you as Exhibit 213, pages 13 and 14. In short, sir, in my submission regreably



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2 these readings don't appear to assist us in determining
3 whether digoxin contributed to this child's death if
4 we accept the validity of Mr. Cimbura's studies.

5 We come then to the case of Andrew
6 Bilodeau. Again there are no ante mortem or post
7 mortem blood specimens available on the child taken
8 within two weeks of death. There were a great variety
9 of tissue specimens tested, all exhumed and in addition
10 this particular child had been embalmed. Mr. Cimbura
11 reported that the levels measured of heart, lung and
12 liver tissues in the child were all within the range
13 of therapeutic concentration, and you will note they
14 were all tested using HPLC.

15 We are in the situation, sir, where
16 the heart, lung and liver tissues were all tested using
17 HPLC and only therapeutic concentrations were reported.
18 Subsequently Mr. Cimbura however tested exhumed brain
19 tissues, again HPLC/RIA, with one exception only, as
20 is set out on the next page, sir, the brain tissue
21 level, with one exception only all levels measured in
22 the brain tissue were higher than those found in fresh
23 brain tissue for children on digoxin therapy. He
24 suggested therefore that the results although
25 inconclusive regarding digoxin toxicity, the measure-
ments in the brain were well within the toxic range.



1
2 Once again in my submission, sir, in
3 the case of Andrew Bilodeau it should be noted that
4 a very large number of tissue specimens were tested
5 and that all of them were tested using HPLC, so that
6 we appear to have conflicting results insofar as
7 digoxin is concerned and that none appeared in the
8 heart and the lung - I am sorry, excuse me, sir.
9 That although they appeared in the heart, lung and
10 liver they were all within therapeutic concentrations,
11 and then we come to the brain tissues and they were
12 in the toxic range.

13 I cannot assist you, sir, as to whether
14 or not the stomach tissue sample is within a toxic
15 or therapeutic range, I have not been provided with
16 that information in Mr. Cimbura's report. Nor can
17 I help you with the intestine readings from either
18 the small or the large.

19 We come then, sir, you will be relieved
20 to know, to the second of the last children, Alan
21 Perreault. We have only one reading on this child
22 at all. It is a post mortem blood specimen that was
23 tested at the Centre of Forensic Sciences and appears
24 to have been taken at autopsy on July the 8th and
25 was tested using HPLC/RIA and no digoxin was detected.
I should say, sir, that the only evidence that we have



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2 with respect to any specimen from this child is a
3 reference in Mr. Cimbura's report to this level. There
4 is no indication, nor in the medical chart of the
5 child, nor as I recall the evidence any direct
6 evidence as to when this specimen was taken, but the
7 indication in Mr. Cimbura's report, 95E at page 5,
8 is that it was reported to him that it had been taken
9 at autopsy and hence was a post mortem sample. He
10 concluded on the basis of the level that the possibility
of digoxin toxicity in this case could be ruled out.

11 We come then to the last of the 36
12 children where toxicological data is available and
13 this is the case of Laura Woodcock who died on June
14 the 30th. There are no ante mortem blood levels
15 taken within two weeks prior to her death. There are
16 no post mortem blood levels at all. The only tissue
17 specimens available, sir, you will see is a muscle
18 tissue and it was exhumed tissue. It was tested on
19 RIA only and even by that system only traces of a
digoxin like substance could be detected.

20 Dr. Kauffman in considering this case
21 expressed the opinion that the traces of digoxin
22 found in Laura's muscle tissue were compatible with
23 the digoxin received by her at Oshawa General Hospital
24 prior to referral to the Hospital for Sick Children.
25



6 1
2 He did however note that this was a reading taken
3 from exhumed tissue many months after burial, and
4 that that could have resulted some 18 months after
5 burial, sir, and it could have resulted in very
6 significant degradation and reduction of the level
7 in the tissue.

8 Dr. Mirkin has testified that given
9 that 18 month period of time between death and
10 exhumation and testing, that the level really doesn't
11 help us very much in determining whether or not
12 digoxin played a part in the child's death.

13 Apart from the actual levels that
14 were measured by Mr. Cimbura, sir, you may recall
15 that various pharmacologists attempted where they
16 thought it possible, despite the limitations, to
17 arrive at certain estimates as to the likely route
18 of administration of digoxin, as to the time of its
19 administration and as to the amount of the dose that
20 might have been given.

21 I note my friend Mr. Brown perusing
22 the index and I can tell him that in the context of
23 continuing education it has been suggested that I
24 deal with this this morning and I intend to be brief
25 and do that.

However, there are two primary things



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2 that should be noted with respect to all of these
3 estimates, sir. First of all it was possible,
4 according to all of the pharmacologists in only a
5 limited number of cases, primarily in the case of
6 Justin Cook, Alana Miller, Kevin Pacsai, Kristin
7 Inwood and Janice Estrella. In some instances through
8 some witnesses some opinions were expressed concerning
9 Stephanie Lombardo, Jesse Belanger and Jordan Hines,
10 but it was certainly not from all the pharmacologists
and certainly not complete.

11 It is my purpose, sir, to review the
12 estimates actually made where they were made and I
13 will not outline the underlying assumptions that were
14 made by the various pharmacologists because they are
15 very numerous. It is fair to say, sir, that with
16 respect to all of these estimates that each of the
17 pharmacologists recognized that the estimates were
18 most certainly not absolutes, that they were as
19 reliable as the assumptions which were their foundation
and it was very difficult to make estimates of this
kind at all.

20 As a general observation of the
21 opinions that have been expressed, sir, in most
22 cases, with the exception of two or three intravenous
23 administrations, it was the preferred explanation
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2 if one assumed that an unprescribed dose of digoxin
3 had been given to the children. There were two
4 exceptions to that and I will deal with those where
5 some experts opined that they thought oral administration
6 was the more likely route.

7 In the case of Dr. Speilberg, and in
8 the case of Dr. MacLeod they felt there were better
9 explanations available for some of these children,
10 particularly Kevin Pacsai, than administration of
11 digoxin.

12 There are two conflicting theories
13 as to the amount of the drug that would be required,
14 again assuming it was given. The first is that one
15 adult ampule would be enough if given by IV bolus
16 shortly before death. That is the opinion of Dr.
17 Speilberg and in some cases Dr. MacLeod. I say
18 immediately, sir, that that is true in some instances
19 with the other pharmacologists, but in Dr. Speilberg's
20 opinion on all the cases that he reviewed that can
21 explain the levels that did result. That is to be
22 compared with the conflicting theory and opinion of
23 some pharmacologists that more than one adult ampule
24 of digoxin would be required to realistically or
25 probably achieve the levels that were measured.

We are in the course of preparing, a



1
2 series of charts on these eight children for you
3 setting out what the evidence of these various
4 witnesses has been, both as to likely route of
5 administration, time and amount of dose. They are
6 not yet complete but when they are Mr. Lamek will
7 provide them to you as he intends to deal with them
8 during his discussion of the various children.

9
10 If we could deal, sir, then with
11 Justin Cook first. Dr. Kauffman - and I should say
12 as well for the benefit of my friends and for you,
13 sir, that the charts will include the references to
14 the transcripts and exhibits so I don't intend to go
15 through them now unless you wish them. With respect
16 to Justin Cook, Dr. Kauffman has testified that the
17 IV route of administration in the lower or distal
18 IV line is the most likely route. He thought oral
19 administration of digoxin was highly unlikely and
20 he thought intramuscular administration was inconceivable
21 in his words.

22 I refer you, sir, to Exhibit No. 266
23 which is Dr. Kauffman's main report, there are two
24 reporting letters prepared to Mr. Wiley of the Crown
25 Attorney's office.

Dr. Spielberg, again dealing with the
question of route, agreed that an intravenous bolus



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2 shortly before death could explain the levels.

3 Dr. MacLeod did not provide any direct
4 opinion on the matter, but discussed intravenous
5 administration only in the context of estimating
6 times and amounts. In my submission he must there-
7 fore be taken to have regarded oral as unlikely and
8 intravenous the more likely route of administration.

9 Dr. Hastreiter thought that an intra-
10 venous bolus administration was more likely than either
11 oral administration or a slow intravenous infusion.

12 When we come to the question of time,
13 sir, the time and amount, the real area of difficulty
14 arises because the opinions are divergent and in some
15 cases very difficult to reconcile.

16 In the case of Cook you will recall
17 sir, that the child arrested at 4:20 in the morning,
18 the onset of his critical symptoms was at 3:45 a.m.
19 and he was pronounced dead at 4:56 in the morning,
20 those are the important times from the pharmacological
21 point of view. There is one other factor I have to
22 add to that, the ante mortem blood sample taken on
23 Justin Cook was taken at approximately 4:30 in the
24 morning and that is the one, sir, you will recall
25 resulting in a high level at the Hospital for Sick
Children.



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Dr. Kauffman on the matter of the likely timing of the dose has testified that it is likely to have occurred between one to three hours before the ante mortem sample was taken at 4:30 in the morning. That puts it, sir, at some time between 1:30 and 3:30 in the morning of March 21st, 1981. He suggests that it had to be more than one hour before the sample was taken because a significant amount of distribution of digoxin from blood into tissue had taken place.

Dr. Speilberg's evidence is somewhat different than that, sir. His basic premise is set out in Appendix 2 to Dr. Bain's report. You may recall, sir, that Dr. Bain's report has been filed as Exhibit 48.

Dr. Speilberg testified that he co-authored Appendix 2 to that report and he has expressed two opinions particular to Justin Cook and others.

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J-1

EMT/hr

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First, as I have suggested, that an intravenous bolus administered shortly before death or prior to or during resuscitation could account for the levels found in five children: Justin Cook, Kevin Pacsai, Allana Miller, Kristin Inwood and Janice Estrella.

Secondly, he has suggested in that appendix that a single adult ampule can account for the levels found in all five of these children.

In fairness to Dr. Spielberg in some cases he thinks there is a better explanation for the levels than the hypothesis of administration of a drug, but assuming administration, those are his views. More particularly in the case of Cook when he testified here and was asked about the likely time frame for administration, he indicated that it was possible that the drug was administered as late as 4:32 a.m. in the morning. To put that in context, sir, that is 24 minutes prior to the death of the child. He suggested - prior to the child being pronounced dead - he suggested that the closer the time of administration to the time of death are more likely than the longer the time away from death.

He also suggested that administration one to two hours prior to death (that is between 2:56



J-2

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2 in the morning and 3:56 in the morning) was possible
3 but he felt it to be less probable.

4 Dr. MacLeod indicated that in his
5 judgement the dose was likely administered 30 minutes
6 or more before death in order to account for tissue
7 levels that were seen. He felt that it was a likely
8 administered between 3:45 in the morning which was
9 the time of onset of Justin Cook's critical symptoms
10 and 4:25 in the morning shortly before the ante mortem
11 blood sample had been taken.

12 He suggested that before 3:45 in the
13 morning becomes less probable unless you are really
14 talking just a minute or two.

15 Dr. Mirkin did not do separate
16 calculations for any of these children with respect to
17 the likely route of administration, time or amount,
18 but he did when invited to do so by counsel express
19 opinions during his evidence. He did not do second
20 calculations for Justin Cook as to the likely time
21 and a likely amount.

22 Dr. Hastreiter has testified that if
23 you assume as he considered likely that the dose was
24 administered by an intravenous bolus it is likely it
25 was administered just prior to the onset of Justin
Cook's critical symptoms.



4-3

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2 Now, when the question was put to Dr.
3 Hastreiter it was suggested that those symptoms had
4 started at 3:30 in the morning. If anything turned
5 on the 15 minutes, sir - it is in fact 3:45 - he is
6 really suggesting, therefore, between 3:15 in the
7 morning and 3:40 a.m. was likely when the dose was
8 administered. Assuming an intravenous bolus. If it
9 was administered orally, which he felt unlikely in
10 this case it could have been accomplished, it was
11 possible that it could have been accomplished at
12 about 2:30 in the morning when we know the child was
fed.

13 When it comes to the calculations of
14 the amount of the dose, sir, I regrettably have to
15 tell you that the evidence is again divergent .

16 Dr. Kauffman calculated both a minimum
17 and a maximum dose in this case and expressed the view
18 in his report to Mr. Wiley and expressed the opinion
19 here that it was likely the amount of the dose was
20 somewhere in between. His minimum which he regarded
21 as unlikely was 10 vials of the pediatric form of
22 digoxin or one adult vial. Inasmuch as he rejected
23 the minimum as being improbable, he therefore rejects
24 the one adult ampule theory, and is suggesting that
25 it would require something more than that to account



J-4

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2 for both the blood and tissue levels.

3 Dr. Spielberg is in direct conflict
4 with this view. He feels that one adult ampule could
5 account for the level if it was administered shortly
6 before death or during the resuscitation effort.

7 He too attempted to estimate a minimum
8 dose but felt it to be an unlikely scenario. He
9 suggested that his minimum was a fraction of a
10 pediatric vial; approximately a third of a pediatric
11 vial. That assumes no distribution from the blood
12 into tissues at all, which is obviously unlikely
13 because we know that there was considerable distribution
14 at least into the fresh heart tissue of this child.

15 His maximum which he described as being
16 extremely unlikely as well was 12 adult ampules and
17 120 pediatric.

18 Dr. MacLeod agreed that one adult
19 ampule could account for the levels in this child
20 so long as it was administered at 3:45 in the morning
21 or thereafter. Again if it was given before 3:45 in
22 the morning he didn't think that it could account for
23 the level in the tissue and serum as well as the fact
24 that the child lived until 4:56 in the morning.

25 Dr. Mirkin was asked during his second
attendance here, sir, whether he agreed with the



F-5

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2 assumptions that had been made by both Drs. Spielberg
3 and Kauffman in attempting to arrive at these estimates,
4 and his general response was his general assumptions
5 within the limitations that those two pharmacologists
6 set out, he did. He, in the context of Justin Cook
7 discussed only the intravenous route of administration,
8 but his opinion as to which was the more likely route
9 was not directly sought, nor as to amount and likely
time.

10 He did, however, say that he thought
11 0.8 milligrams of the drug was a not unlikely dose.
12 That is more than one adult ampule - in fact it is
13 almost 2 - and it is a considerable number of pediatric
ampules.

14 Then finally, sir, on this child --
15 Dr. Hastreiter has expressed a number of opinions on
16 all of these children. You will recall that he
17 testified at the preliminary hearing where he postulated
18 in many cases and specifically in the case of Justin
19 Cook that a large number of ampules would have been
20 required to account for this child's level.

21 When he testified here, sir, he
22 indicated that his calculations and his opinions as
23 expressed at the preliminary hearing were based on
24 the assumption of steady state concentrations which
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JP-6

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he in fact felt to be an unlikely scenario.

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When he testified here, sir, he expressed a minimum of likely dose for Justin Cook as being 0.5 milligrams which is one adult ampule of digoxin or 10 pediatric.

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His maximum as expressed was 1.2 or 1.2 milligrams which is approximately - a little bit more than one adult vial. Sorry, it is actually two adult vials and it is 20 pediatric vials.

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Sir, I propose to briefly go through the same exercise on the remaining children and then Mr. Lamek will have further submissions to make to you starting this afternoon. I can attempt to complete Allana Miller now or we can start again after lunch.

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THE COMMISSIONER: We will rise now until 2:15.

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--- Luncheon adjournment.



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AA

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--- Upon resuming at 2:15 p.m.

EMT/wb

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THE COMMISSIONER: Yes, Miss Cronk?

2:15 p.m.

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MS. CRONK: Thank you, sir.

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Sir, before we move on to the

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estimates that were made in the case of Allana Miller,

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I think I can now provide you with a breakdown on

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those 12 children that we discussed earlier this

9

morning.

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THE COMMISSIONER: Yes. All right,

thank you.

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MS. CRONK: You will recall, sir,

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that I said on selected samples from each of those

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12 children Mr. Cimbura reported a range within

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the toxic range. The breakdown on each of the

15

children is as follows:

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In the case of Justin Cook, his blood

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levels were exclusively in the toxic range. His

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fresh heart tissues were exclusively in the toxic

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range. His fixed heart tissues were exclusively

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in the therapeutic range. His fresh lung tissue was

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50% higher than the upper end of the toxic range.

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THE COMMISSIONER: The upper end

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of the toxic range?

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MS. CRONK: The toxic range, sir.

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AA2

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THE COMMISSIONER: Then it was
certainly toxic.

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MS. CRONK: Well, a little beyond,
sir; 50%.

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THE COMMISSIONER: It can't be beyond
the toxic range. I can't accept that --

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MS. CRONK: I understand what you are
saying, sir. The number reported was 50% higher
than the highest previously reported.

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THE COMMISSIONER: All right.

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MS. CRONK: In the case of Kevin
Pacsai, sir, his ante mortem and post mortem blood
specimens were exclusively in the toxic range. His
fixed heart specimen from the left ventricle was in
the overlap range. His fixed septum tissue
specimen was exclusively in the therapeutic range.
His fixed lung tissue was exclusively in the toxic
range. His frozen lung specimen was exclusively
in the toxic range.

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In the case of Allana Miller, her
blood specimens were exclusively in the toxic range
but they were assayed on RIA only.

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In all these other cases, sir, unless
I indicate to the contrary, HPLC plus RIA was used.



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In the case of Kristin Inwood, her post mortem blood level was exclusively in the toxic range. Her heart tissues, the left ventricle was in the overlap range. The left atrium was in the therapeutic range. The septum was in the overlap range. The thigh muscle was exclusively in the toxic range.

In the case of Jordan Hines, both specimens from the heart, the fixed heart, were exclusively in the therapeutic range. His exhumed liver specimen was exclusively in the toxic range but was assayed by RIA only. His fixed lung specimen was in the overlap range.

With Colleen Warner, her fixed left ventricle specimen was in the overlap range. The other two heart specimens, both fixed, were exclusively in the therapeutic range.

In the case of Charlon Gardner, her fixed heart specimen from the left ventricle was in the overlap range. The measurement in the left atrium of the heart (that is fixed) was below the therapeutic level set out by Mr. Cimbura and reported --

THE COMMISSIONER: The same comment on that, too.



AA4

1 MS. CRONK: That's right. The septum
2 specimen, fixed heart, was in the overlap range and
3 her fixed lung specimen was exclusively in the toxic
4 range.

5 Jennifer Thomas, her fixed lung
6 specimen was exclusively in the toxic range. Her
7 fixed heart specimens were exclusively in the
8 therapeutic range.

9 With Matthew Lutes, his fixed lung
10 specimen was in the overlap range. His left
11 ventricle in the heart and his septum specimen from
12 the heart disclosed no digoxin. And his left atrium
specimen was exclusively in the therapeutic range.

13 Stephanie Lombardo, exhumed heart
14 specimens, both were in the overlap range. Her
15 exhumed liver specimen was exclusively in the toxic
16 range. Her exhumed lung was exclusively in the
17 toxic range and exceeded the maximum reported in
the literature in the toxic range.

18 With Barbara Gionas, her exhumed
19 heart specimens were both in the overlap range. The
20 exhumed liver specimen was exclusively in the toxic
21 range. The exhumed lung specimen, both from the
22 right and left lung, were in the exclusively toxic
23 range.
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With Jesse Belanger, the exhumed liver was exclusively in the toxic range.

The breakdown then of all 12, sir, is as follows: in all 12, there was at least one level exclusively within the toxic range.

THE COMMISSIONER: What about Colleen Warner?

MS. CRONK: I'm sorry, sir, with the exception of Colleen Warner. I'm sorry, may I restate that? In all 12 cases, there was at least one level within the toxic range; not necessarily exclusively. It could have been in the overlap area.

THE COMMISSIONER: Within the overlap, yes.

MS. CRONK: With Cook, there were three levels exclusively toxic. With Pacsai, there were three levels exclusively toxic and one in the overlap range.

With Miller, one level exclusively toxic but measured by RIA only.

With Inwood, two levels exclusively toxic, plus two in the overlap range.

With Hines, one level exclusively toxic but measured by RIA only and one in the overlap range.



AA6

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With Warner, as you point out, one in the overlap range. With Gardner, one exclusively toxic, two in the overlap range.

With Thomas, one exclusively toxic. With Lutes, one in the overlap range. And to that should be added as a thirteenth child, sir, Estrella. If one assumes that the post mortem pelvic cavity reading can be relied upon, it is clearly exclusively within the toxic range.

Could I turn now to the estimates that were made in the case of Allana Miller, both as to the likely route of administration, time of dose and amount of dose, assuming an unprescribed dose of digoxin was in fact administered.

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BB-1

RD/ac

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2 Dr. Kauffman in this case, sir, indicated that in
3 his opinion an intravenous bolus injection was
4 the most likely route of administration, that oral
5 was unlikely and when he first appeared and testified
6 before you, sir, he gave evidence that administration
7 through the intravenous bottle or buretrol was in
8 his opinion unlikely.

9 As you recall, sir, he was asked to
10 deliver a report in light of the evidence of
11 Bertha Bell concerning her observations the night
12 of Allana Miller's death. In his opinion, in light
13 of Miss Bell's evidence, on the assumptions outlined
14 by him in Exhibit 404, was that administration was
15 possible through the intravenous buretrol if the
16 dose was given using a 3 cc. syringe and was
17 administered at approximately 11:51 p.m.

18 Dr. Spielberg testified that he
19 thought a single intravenous bolus shortly before
20 death would account for the child's levels. That
21 is found, sir, in Dr. Bain's report at Appendix 2,
22 page 39.

23 Dr. MacLeod's preferred route was
24 not precisely sought from him, but his evidence
25 concerned only intravenous route circumstances.
That was true, as well, of Dr. Hastreiter's evidence



SB-2

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2 here before you.

3 With respect to time, Dr. Kauffman
4 indicated that if it was an intravenous bolus
5 it was most likely administered within 60 to 90
6 minutes of the onset of Allana Miller's critical
7 symptoms, which occurred at 1:45 a.m. His best
8 view was that it was likely within an hour of
9 1:45 in the morning. If, however, it was a slow
10 intravenous infusion, on his evidence, it could
11 clearly have been as early as 11:51 p.m. on the
12 assumption that he outlined in his letter.

13 Dr. Spielberg, and I should say,
14 sir, in outlining all of the this evidence, there
15 are a great number of references in the evidence
16 from all of the pharmacologists, Dr. Spielberg
17 indicated that an IV bolus shortly or before
18 arrest or at the arrest could account for the
19 child's levels. Dr. MacLeod agreed with Dr. Spielberg
20 in the results but didn't think that an estimate
21 was really possible with any degree of confidence,
22 as to the likely time.

23 Dr. Hastreiter testified that if
24 the dose had been given intravenously he thought it
25 would have been given 5 to 30 minutes prior to the
arrest at 2:45 in the morning, but it could also



BB-3

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2 have been given 5 to 30 minutes prior to the onset
3 of the critical symptoms at 1:45 in the morning.

4 Once again, sir, there is a
5 variation in the estimates as to amount. Dr. Kauffman
6 indicated that if it was an IV bolus the minimum
7 that would be required was one adult vial or 11
8 pediatric ampules. If it was administered through
9 the IV buretrol that minimum dose became more
10 unlikely and a larger dose would be required, although
11 he didn't specify the amount. Dr. Spielberg, of
12 course, indicated that one adult ampule could account
13 for the levels. He additionally went on to say
14 that a minimum amount of less than one pediatric
15 ampule was, in fact, possible given the low tissue
16 levels in Allana Miller, although he thought it
17 unlikely. Dr. MacLeod indicated that it wasn't
18 really possible to make an estimate. Dr. Hastreiter
19 gave us an estimate, assuming non-steady state and
20 he indicated one adult ampule or slightly more.

21 We come to Kevin Pacsai, sir, and
22 there is an area of dispute, both as to the likely
23 route of administration and as to the times.

24 Dr. Kauffman indicated that he
25 really couldn't distinguish in terms of likelihood
between the oral or the intravenous route. At one



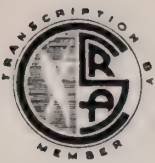
BB-4

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2 point during his evidence, when he was asked to
3 state a preference that he must, he indicated oral
4 administration. At another point in his evidence
5 when asked a similar question, he indicated
6 intravenous. He did, however, say in his opinion
7 that an IV bolus was unlikely if given shortly before
8 the onset of Kevin Pacsai's symptoms.

9 In this case, sir, you will recall
10 that there is an issue as to when the critical
11 symptoms in fact commenced. According to one of
12 the nursing notes in the chart it could have been,
13 you could consider it to be 4:00 in the morning,
14 and alternatively, it could be 5:30 in the morning,
15 which is the time that Dr. Costigan made his note
16 about having been called to see the child and with
17 respect to his arrangements to transfer the child
18 to the intensive care unit.

19 Dr. Kauffman indicated that if it
20 was an intravenous dose that route of administration
21 was possible if it was administered three to six
22 hours prior to the onset of the critical symptoms.
23 Again, it depends on what you consider to be the
24 onset.

25 Dr. Spielberg testified, both with
respect to the intravenous and the oral methods, but



BB-5

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2 generally with respect to this child, as well,
3 he felt an intravenous bolus of a single adult
4 vial could account for the levels. Dr. MacLeod,
5 however, indicated that if the dose had been
6 administered prior to 5:30 a.m. it was almost certainly
7 the oral route. He felt the oral route to be
8 more likely and if the administration had taken
9 place prior to the onset of symptoms, which occurred
10 at the latest by 5:30 in the morning, the intravenous
11 route was unlikely, having regard to the length of time
12 that the child survived before being pronounced
13 dead.

14 Dr. Hastreiter has testified in
15 his opinion that an intravenous bolus was most likely
16 the route of administration.

17 On times of dose, sir, Dr. Kauffman
18 has testified that if it was given orally the earliest
19 time would be 4 to 5 hours before the onset of
20 symptoms. If intravenously, the earliest time would
21 be 1 to 2 hours before onset, but he did not think
22 that he could be specific under this assumption, that
23 is route of administration.

24 Dr. Spielberg indicated that if it
25 was an oral dose, if the sample, the ante mortem
sample from Kevin Pacsai was taken while the level



BB-6

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2 of digoxin was still rising, the earliest the
3 dose could have been administered would be 1 to 3
4 hours before the sample. You will recall, sir,
5 that Dr. Costigan has indicated that he took the
6 sample between 6:00 in the morning and 6:30. That
7 would make the time then roughly 3:30 to 5:30 in
8 the morning for administration. If, however, the
9 sample was taken when the level was decreasing,
10 that is when distribution in the Alpha Phase had
11 started, he didn't feel he could estimate a time.
12 If it was an IV bolus that was administered to the
13 child, as he thought was likely, it could have been
14 administered prior to or during the resuscitation
15 effort.

16 Dr. MacLeod indicated that it was
17 possible that there was administration anywhere
18 from seconds to hours before 5:30 in the morning,
19 picking that as the onset time. If however it was
20 oral administration, which he felt to be more likely,
21 he felt it was administered before 5:30 in the morning,
22 and likely 1 to 2 hours before.

23 With Dr. Hastreiter, if it was an
24 intravenous bolus he felt it would be between 3:30
25 and 3:55 in the morning, assuming the onset of
symptoms at 4:00 a.m.



BB-7

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2 With respect to the amount that
3 was postulated, sir, by the various witnesses, again
4 we have a broad discrepancy. Dr. Kauffman indicated
5 that a minimum oral dose would require a dose of
6 .719 milligrams in a volume of 14 millilitres of
7 elixir. Dr. Spielberg, of course, said that a
8 single vial of adult IV preparation. Dr. MacLeod
9 indicated that if it was intravenous one adult
10 ampule administered close to 5:30 a.m. could account
11 for the levels. If it was an oral administration
12 2 or 3 millilitres of elixir would be required.

13 Dr. Hastreiter at non-steady state
14 didn't provide an exact amount, but indicated it
15 clearly had to be more than a therapeutic dose.
16 It was clearly an overdose amount in his judgement.

17 Dealing with the case of Stephanie
18 Lombardo, sir, Dr. Kauffman has testified that both
19 with respect to both route, time and likely amount,
20 it is very difficult to make a reasonable estimate,
21 but it was possible that it could have been either
22 orally or intravenous bolus by way of a rapid
23 infusion. He thought it was more likely an intravenous
24 administration than an oral administration.

25 Dr. Hastreiter indicated that the
probability of oral administration was fairly high,



BB-8

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2 could in fact have been given during the child's
3 feedings at 1:30 and 3:00 in the morning, the time
4 of her death. Neither has Dr. Spielberg or Mirkin
5 expressed a direct opinion as to the referred route
6 in this case.

7 There is however a direct conflict,
8 if you will, on the evidence of the pharmacologists
9 concerning the likely time of the dose. Dr. Kauffman
10 has said that although he really doesn't, didn't
11 feel that he could make a reasonable estimate on
12 the known data as to the likely time, it could have
13 happened at any time after her transfer to ward 4A/B.

14 Dr. Spielberg suggested that it
15 could have happened at anytime during her last
16 hospitalization at the Hospital for Sick Children.
17 It was also conceivable that it occurred shortly
18 before or during resuscitation, notwithstanding
19 the degree of distribution in tissues.

20 You will recall, sir, that Stephanie
21 Lombardo was hospitalized for approximately 35 days
22 at the Hospital for Sick Children before her death.
23 In light of Dr. Spielberg's evidence, Dr. Kauffman
24 was directly asked whether or not he agreed it
25 could have been administered at any time over the
course of those 35 days and still account for the



BB-9

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2 child's symptoms, manner of death and the levels
3 achieved. He testified that he felt it hard to
4 accept that it was given prior to three days before
5 death, that it was inconceivable that it was given
6 ten days prior to death.

7 THE COMMISSIONER: I'm sorry,
8 who said that?

9 MS. CRONK: Dr. Kauffman. He felt
10 the dose was probably given within one hour of the
11 onset of the child's critical symptoms. If, in fact,
12 an intravenous bolus was used it could have been
30 or 60 minutes prior to death.

13 Dr. Hastreiter testified that he
14 thought the earliest time was two hours before the
15 onset of critical symptoms which would make
16 administration at or about 1:30 with onset at
3:30.

17 Dr. Mirkin indicated that in his
18 judgement it depended on the particular route. He
19 gave a different estimate depending if it was oral,
20 depending if it was intravenous. If oral, one and
21 a half hours to two hours before the onset of
22 symptoms, which puts him closely in the framework
23 of Dr. Hastreiter. If intravenously, 5 to 30 minutes
24 before the onset of critical symptoms.
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BB-10

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2 With respect to the amount most
3 of the pharmacologists said that they were unable
4 to estimate an amount at all. Dr. Hastreiter
5 indicated simply that it would require more than
6 one therapeutic or more than one maintenance dose.
7 Dr. Mirkin indicated that one adult vial could
8 account for the levels.

9 I come then to Jesse Belanger, sir.
10 Dr. Kauffman has said in this case, once again,
11 it is virtually impossible on the known data to make
12 an estimate on any of these aspects. Drs. Mirkin,
13 Spielberg, MacLeod and Hastreiter expressed no
14 opinion as to which was the more likely route of
15 administration, oral versus intravenous. When it
16 came to time, however, several of the witnesses did
17 attempt to provide an estimate. Dr. Kauffman indicated
18 that it was possible, but unlikely that it had been
19 given at any time during the child's hospitalization
20 at the Hospital for Sick Children. That arose
21 again, sir, because Dr. Spielberg testified that
22 he felt the dose could have been administered at
23 any time during the child's last hospitalization
24 and still accounted for the levels. Dr. Kauffman
25 admitted it was possible, but thought it was unlikely.
He said that it could have been given at any time on



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wards 4A/B at five hours prior to death.

Dr. Mirkin indicated that if it was oral administration, administration one and a half to two hours prior to the onset of critical symptoms at 6:30 would account for the levels. If intravenously, 5 to 30 minutes before the onset.

Finally, when we come to the amounts, sir, Dr. Mirkin has weighed in for one adult vial. Drs. Kauffman and Spielberg felt unable to estimate an amount. Dr. MacLeod didn't express one and Dr. Hastreiter again said that it would require more than one maintenance dose.

We have three more children, sir. I will try to move through them quickly.

Kristen Inwood, Dr. Kauffman again indicated that it wasn't possible to estimate with any degree of certainty based on known data. He thought the intravenous route was somewhat more likely than the oral route. Dr. Spielberg expressed the opinion that an intravenous push administration shortly before death was the most likely scenario. Dr. MacLeod indicated that there was a high degree of certainty; it was not the oral route.

With respect to the timing of the dose Dr. Kauffman indicated that if it was a single intravenous



BB-12

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2 dose it was unlikely to have been administered
3 earlier than three to four hours prior to the
4 onset of the symptoms, which occurred at 2:00 in
5 the morning. He also indicated that administration
6 between 2:00 and 2:30 in the morning, in his
7 judgement, could not account for the tissue levels
8 or the serum levels found in this child, again
9 assuming intravenous administration.

10 Dr. Spielberg, however, has
11 testified that the dose could have been administered
12 very close to the time of arrest and death and, indeed,
13 he felt this to be most likely in the circumstances
14 of this case. If it was a very large dose the
15 earliest time for administration would have been
16 four hours before the arrest, which you will recall,
17 sir, occurred at 2:30 in the morning. That would
18 make the earliest time approximately 10:30 p.m.

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CC
MT/cr

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2 Dr. MacLeod again provided earliest
3 and latest estimates at the request of counsel. The
4 latest time he thought was a few seconds before arrest,
5 assuming that one adult vial had been used. The
6 earliest time in his judgment was not earlier than
7 minutes or seconds before 2 o'clock in the morning, again
8 assuming one adult vial. In his best judgment
9 administration had occurred probably close to the time
10 of death.

11 Dr. Hastreiter indicated that one and
12 a half hours prior to death was his best estimate,
13 assuming the onset of symptoms at approximately 2
14 o'clock in the morning.

15 When we come to amount, sir, we have
16 the same difficulty. Dr. Kauffman declined to
17 estimate an amount on the known data. Dr. Speilberg
18 indicated that we had to consider it at two different
19 points in time; one as if the drug was still in the
20 central volume of distribution and still distributing
21 out to tissues, in which case two and a half adult
22 vials could have accounted for the levels. If in
23 fact it was, as he suspected, immediately before the
24 cardiac arrest less than one adult vial could account
25 for the levels.

With no distribution at all in the
tissues one full paediatric vial or a fraction of



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2 an adult vial.

3 Dr. MacLeod agreed that one adult
4 vial was possible to explain the levels if arrest
5 had followed shortly thereafter.

6 Dr. Hastreiter indicated his minimum
7 amount was 1.3 milligrams approximately an hour and
8 a half prior to death. If it was given longer than
9 that, that is three hours prior to death, the minimum
amount goes up to three and a quarter milligrams.

10 With Janice Estrella when we come to
11 examine the route, Dr. Kauffman testified that the
12 oral route is highly unlikely, and it was most likely
13 a large intravenous bolus. I should say, sir, that
14 at the time that Dr. Kauffman delivered his initial
15 reports to Mr. Wiley he was not aware of the source
16 of the pelvic cavity sample, so these estimates were
17 given assuming that pelvic cavity sample to
accurately represent a post mortem blood level.

18 Dr. Speilberg indicated that an IV
19 bolus shortly before death could account for this
20 child's levels.

21 Dr. Hastreiter indicated that a slow
22 intravenous infusion was possible below the buretrol,
23 but he thought it was less likely than lower down on
24 the IV line. Neither Dr. Kauffman nor Dr. Speilberg
25



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2 provided any direct estimate as to the time of
3 administration, nor did Dr. MacLeod or Dr. Hastreiter,
4 when he appeared before you. The amount of the dose
5 however was canvassed with each and Dr. Kauffman
6 indicated that if it had been given intravenously the
7 minimum dose was six paediatric ampules or less than
8 one adult ampule. If given orally the minimum dose
9 was approximately a teaspoon of .3 milligrams of
10 the elixir but he felt that it was somewhere likely
higher than that by virtue of the intravenous route.

11 Dr. Speilberg again said that less
12 than one adult vial and more than one paediatric
13 vial was a reasonable possibility.

14 Dr. Hastreiter testified at the
15 preliminary hearing with respect to steady state
16 figures, it does not appear to be given here, sir,
17 an estimate based on the non-steady state. If you
18 are assuming steady state we are talking about three
and a half adult as a minimum or 10 plus paediatric.

19 Finally, sir, we come to the case of
20 Jordan Hines. Once again given what he considered to
21 be the limited data available, Dr. Kauffman felt it
22 was impossible to estimate a preferred route of
23 administration, the timing of dose or the amount of
24 dose.
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2 Dr. Speilberg agreed that it was not
3 possible to estimate a route. When it came to time,
4 however, Dr. Speilberg indicated that it was possible
5 the dose was administered before or during the
6 resuscitation effort on this child. Dr. Kauffman
7 disagreed when that evidence was put to him.
8 According to Dr. Kauffman, if an oral dose had been
9 used it was unlikely to have been administered
10 earlier than five hours prior to the time of arrest,
11 that is not earlier than 11:10 p.m. on March the
12 7th. If administered intravenously it was unlikely
13 administered earlier than three hours prior to the
14 time of the arrest.

15 Dr. MacLeod confirmed Dr. Speilberg's
16 view that it was possible the drug had been
17 administered at any time during Jordan Hines
18 hospitalization at the Hospital for Sick Children.

19 Dr. Hastreiter indicated that it was
20 impossible to estimate the time but he thought the
21 latest at which it could have been given was
22 approximately 2:10 in the morning assuming onset of
23 critical symptoms at approximately 4:10 in the morning
24 as disclosed by the medical record.

25 The opinions expressed with respect
to the amount of the dose, sir, are perhaps scantier



Cronk (Argument)

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2 than in other cases.

3 Dr. Kauffman indicated it was unlikely
4 to have been a single therapeutic dose.

5 Dr. Speilberg indicated it wasn't
6 possible to estimate.

7 Dr. Hastreiter indicated that it could
8 be as little as one loading dose.

9 I have said, sir, that there are charts
10 being prepared containing that information and the
11 various transcript references and as soon as they
12 are available we will distribute them to counsel.

13 There is one other area that I propose,
14 sir, to touch upon briefly today before Mr. Lamek
15 returns to take over the guard if you will, and that is
16 the evidence that you have heard with respect to the
17 treatment of digoxin at the Hospital for Sick
18 Children, the forms in which it was available during
19 the enquiry period, the rules that applied to its
20 storage and the rules and procedures that applied as
21 to who might administer it and under what circumstances.

22 As you know, sir, during the nine
23 month period with which we are concerned digoxin was
24 not a controlled drug on Wards 4A/4B. It did not
25 become one until the night of March the 21st, 1981.
All forms of the drug were therefore available on the



wards as ward stock. Stock medications were generally provided to the ward by prescription and this applied as well to digoxin. It was available, sir, in three forms. In the elixir which we have heard came in the 100 millilitre bottle volume with a concentration of 0.05 milligrams per millilitre. The bottle was at that time dark in colour, the drug itself was light green in colour. It was available obviously in ampule form, the paediatric ampules came in a 1 millilitre volume with a concentration of 0.05 milligrams per millilitre. The adult ampule came in a 2 millilitre volume with a strength of .25 milligrams per millilitre. The adult you will recall, sir, was therefore two times the volume and five times the concentration of the paediatric.

Dr. Rowe has provided those figures to us, sir, and as well they are set out in the Atlanta Report which has been filed as an exhibit.

We have heard as well, sir, evidence concerning the packaging of the ampules during the enquiry period, and as well examples as you know have been marked as exhibits. It appears that the paediatric ampules came in boxes of 10, the boxes had black lettering on a white background. The adult ampules came in boxes of five and the boxes had red



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lettering on white background.

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The third form in which the drug was available was in tablet form, sir, it was available in two concentrations, either 0.25 milligrams or 0.125 milligrams.

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Digoxin and other drugs during the nine months were kept in each of the medication rooms on 4A and 4B. In each room there was a narcotics' cupboard, an unlocked cupboard, open shelves and a refrigerator. We have heard evidence from Mary Costello that ward stock medications including digoxin were stored on the open shelves in alphabetical order, and that the ampules were stored in boxes. Marked as exhibits at the preliminary hearing, sir, were as you know a series of photographs that were taken on Wards 4A/4B, they had been referred to in our exhibit book as Exhibit 32A, B and C, but copies of the photograph are not reproduced in this book. I am going to show you the originals, sir, and I am referring to Exhibit 29C at the preliminary hearing, 29D and 1M.

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You will see, sir, these photographs were taken by a police photographer with the Metropolitan Toronto Police Force, they were not taken during the nine month period but rather in December



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2 1981 and January 1982. While the copies of the
3 photographs, sir, are not terribly clear I introduce
4 them for two purposes. First you will see, sir, that
5 in light of the evidence that Mary Costello, and the
6 issue as to whether or not these drugs were stored
7 alphabetically, it appears that arrest drugs were
8 kept on the top shelf and they do appear to have been
9 filed in an effort to do so alphabetically, although
10 in some cases stored alphabetically under the generic
11 versus trade name.

12 On the next shelf ward stock medications
13 were stored. You will not see digoxin in any of these
14 photographs given that they were taken in December
15 1981 and January 1982 when by that time digoxin had
16 become a controlled drug. Again you will see there
17 appears to have been filing of the drugs alphabetically
18 although in some cases the trade name versus the
19 generic name was used for filing purposes.

20 THE COMMISSIONER: Which is Inderal?

21 MS. CRONK: I can give you the other
22 name, it is my understanding --

23 THE COMMISSIONER: Propanolol is the
24 generic name.

25 MS. CRONK: I think that is right, sir,
propanolol is the other name.



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THE COMMISSIONER: Then they are certainly catering to the manufacturer.

MS. CRONK: You will see as well, sir, I think the second point of significance --

THE COMMISSIONER: Gentamicin is a trade name?

MS. CRONK: As I understand it, sir, it is, that's right, and you might wish to look at Ampicillin and Lasix as well. Perhaps we can then pass the photographs around for other counsel, the copies are somewhat difficult to read.

You will see sir, for example, that on Exhibit No. 1M that the third drug over, 1M, sir --

MR. SCOTT: Is yours easier to read?

THE COMMISSIONER: I have got the original, I am cheating.

MR. SCOTT: I was just stunned at your capacity.

MS. CRONK: Mr. Scott has been away too long, sir. You will see that the third drug over on the second row, sir, is Gentamicin.

THE COMMISSIONER: That is the trade name is it not, Gentamicin?

MS. CRONK: That is my understanding, and beside that, as I read it Heparin filed under H



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2 and beyond that I have difficulty but I think it is
3 Lasix.

4 THE COMMISSIONER: Lasix, yes.

5 MS. CRONK: The other point of interest
6 in the photograph, sir, is that we have heard evidence
7 that with the ampules of digoxin they were filed as
8 I suggested a moment ago in boxes either of 10 or 5
9 depending on the size, 10 if it was paediatric and
10 5 if it was adult. You will note from the way these
11 drugs appear to have been stored that there are in
12 fact larger boxes and the various drugs were kept
13 inside of those, so it may help, sir, to put it in
14 some kind of context.

15 Perhaps we can pass these to other
16 counsel.

17 THE COMMISSIONER: Pass those back
18 to Mr. Scott.

19 MS. CRONK: In addition to the drugs
20 that were kept in the medication rooms, sir, as you
21 know there was a crash cart, a resuscitation cart on
22 each of Ward 4A and 4B where emergency medications
23 were kept. All witnesses from the Hospital for Sick
24 Children familiar with the cardiac wards who testified
25 before you, sir, were unanimous in their evidence
that digoxin was not kept on the crash carts on Wards



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2 4A/4B during the enquiry period, save for two
3 witnesses Dr. Fowler and Carol Browne, both of whom
4 testified that they understood it was kept on the
5 crash cart. Miss Browne admitted however, that she
6 had never seen it there.

7 In addition to the evidence of all of
8 the other Hospital for Sick Children witnesses, there
9 is as well, sir, documentary evidence before you as
10 to whether or not digoxin was likely to have been kept
11 on the crash carts, or indeed whether it was. You
12 will recall, sir, that an inventory list, a photograph
13 of an inventory list of the drugs kept on the 4A/4B
14 crash carts has been filed as Exhibit 295 and the
15 inventory makes no reference to digoxin.

16 You may recall as well, sir, that
17 digoxin is not included in the list of cardiac
18 resuscitation drugs that are listed at the back of
19 the Residents Handbook of Paediatrics, which has been
20 filed, and similarly it is not included in the list
21 of drugs in the handbook for use in situations of a
22 cardiac arrest. Dr. Rowe has testified he couldn't
23 think of a situation, it wouldn't commonly be used in
24 an arrest, it is not intended for that purpose and
25 couldn't think of a situation where it would be.

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And then finally, sir, Dr. Costigan has testified that when he and Dr. Mounstephen performed their digoxin inventory on the evening of March 21st, 1981, they found no digoxin on the crash carts from either 4A or 4B. A copy of their inventory has been filed as Exhibit 205, sir.

As a result both of the documentary evidence and the evidence of most of the witnesses from the Hospital for Sick Children, sir, in my submission there is no real issue. It appears unlikely that digoxin during this period of time was on the crash cart on either of those wards.

Quite apart then from the availability of the drug from one of two sources (that is the medication room on either 4A/4B or on the crash cart) we have heard evidence from a number of nursing witnesses as to the practice of borrowing drugs in circumstances where there was a drug shortage on the wards.

It appears that this occurred on an informal basis; that if 4A was short of a drug, according to Mrs. Radojewski, the nurses from that ward would likely first go to 4B to see if the drug was available and vice versa. And as well strictly as a matter of physical convenience, Ward 4C and 4D were



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2 available on the same floor.

3 The importance or significant feature
4 of that practice in my submission, Mr. Commissioner,
5 is that as a non-controlled drug if digoxin was
6 borrowed by anyone from another ward there was no
7 record kept either of the borrowing or of the lending.

8 There was also a further way in which
9 digoxin during this nine month period could have been
10 obtained in the Hospital, and on those wards.

11 Prior to September, 1980, we have
12 heard that a Registered Nurse from either of the
13 two wards could have obtained digoxin by ordering
14 it directly from the pharmacy. In doing so she did
15 not have to advise the pharmacy as to the identity
16 of the patient for whom the drug was intended, nor
17 for the purpose for which it was intended.

18 You have heard, sir, though, from
19 Mrs. Radojewski that in September, 1980, a clinical
20 pharmacist was assigned to Wards 4A/4B. When she
21 was not on duty, largely on the weekends and for
22 part of the evening and night shift, a Registered
23 Nurse could still order the drug directly from the
24 pharmacy although in the circumstances it would involve
25 the nursing supervisor.

When the pharmacist was on duty it was



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2 her responsibility to keep the ward stock up to the
3 required volumes, and that included digoxin.

4 Before and after September, 1980, sir,
5 there was no record kept on 4A/4B on any basis, be it
6 daily or monthly, recording exactly how much digoxin
7 was in fact used on those wards and in what form. Ward
8 requisition forms recording how much was ordered from
9 the pharmacy was kept for only a month or two and
then discarded.

10 I refer you, sir, to the evidence
11 before you of Mrs. Radojewski at Volume 115, page 6010
12 and 6034, and as well to the evidence of Ms. Umali
13 at the preliminary hearing, Volume 23.

14 There was, however, sir, a ward quota
15 during the nine month period for all ward stock
16 medications including digoxin. According to Mrs.
17 Rappaport the ward pharmacist who testified at the
18 preliminary hearing the quota for digoxin was
19 approximately one 100 millilitre bottle of elixir,
20 10 pediatric ampules and 5 adult ampules for each of
21 Wards 4A and 4B. Her evidence, sir, is found at
Volume 19 of the preliminary hearing.

22 THE COMMISSIONER: What does the quota
23 mean, what they are supposed to use?

24 MS. CRONK: That is the amount that was
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2 as a matter of routine sent up to the wards on a
3 monthly basis subject to, after September, 1980, the
4 ward pharmacist altering the order by ordering more
5 or ordering less. And you will recall, sir, that
6 some of the ward requisition forms have been marked
7 as exhibits before you as they were at the preliminary
8 hearing.

9 Mrs. Radojewski the Head Nurse on Ward
10 4A was unaware, sir, when asked whether or not there
11 had been an increase in the amount of digoxin that
12 had been used on Ward 4A/4B during the inquiry period.
13 She did, however, indicate that she felt that the
14 ward pharmacist after September, 1980, would have
15 noticed an increase if there had been one by virtue
16 of the requisition forms that it was her job to
17 complete.

18 THE COMMISSIONER: Even assuming the
19 worst that all of these children were killed with an
20 overdose of digoxin, that is not a great deal of
21 digoxin, is it, considering the amount that was
22 being used?

23 MS. CRONK: Well, sir, it would depend
24 on the route, sir, and it would also depend on whether
25 the assumptions are made at steady state or non-steady
state.



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THE COMMISSIONER: What amount - do we have any evidence anywhere of the total amount that was used per week in the ordinary course?

MS. CRONK: No, that is the part that I am having some difficulty trying to make, sir. There was no record kept and therefore there is no evidence before you as to the amount that was in fact used, whether it be on a weekly basis or daily basis or monthly basis.

The evidence that is before you is to the amounts that were ordered from the pharmacy after September 1980, and those requisition forms are not complete.

THE COMMISSIONER: All I am saying is that the 36 babies, if poisoned by an overdose of digoxin may only amount to 36 adult ampules; isn't that right?

MS. CRONK: It could, sir. It depends on the evidence of the pharmacologists, whichever you prefer.

THE COMMISSIONER: Would that be noticed in any event?

MS. CRONK: Well, the evidence before you relates to a perceived increase in use, and the other evidence before you by Mrs. Radojewski is that she



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thought that it would be if there was an increase in use. That doesn't resolve the question of whether or not it would in fact be an increase and thus detectable.

THE COMMISSIONER: All I am wanting is how much increase would be necessary to poison 36 children? How much would that be spread over a period of nine months?

MS. CRONK: In my submission, sir, you can interpret the evidence of the pharmacologists in one of two ways: it may in fact not be a significant amount at all if you accept an adult ampule or less theory. It could be a much larger amount if you were to prefer Dr. Hastreiter's evidence about steady state concentration.

THE COMMISSIONER: Even if it is a much larger amount, make it 72 -

MR. SCOTT: It is 80 per patient times 36.

MS. CRONK: Well, without the help of my friend's mathematics we are talking about a great number of -

MR. SCOTT: We are talking Hastreiter; the early Hastreiter, if I can put it that way, said that dealing with one case that 80 ampules would be required. Now the only way you could logically go from that is



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2 to multiply 80 times 36 and you get some sense of
3 volume. Now I don't know how many are in box but I
4 am sure Miss Cronk in her notes has that somewhere.
5 But over nine months, who is to say, but it is not a
6 modest amount. On that theory.

7 MS. CRONK: It depends on the theory,
8 sir.

9 THE COMMISSIONER: If you are taking
10 that theory that has been expressed by several
11 witnesses that it would take only one adult ampule,
12 if that was one per 36, that is 36 adult ampules.
13 I don't know how many they use in the ordinary course
14 of the week.

15 MS. CRONK: There is evidence before
16 you, sir, as to the number, the approximate number
17 of doses given in a month of digoxin in the Hospital
18 but not particular to Wards 4A or 4B. Indeed the facts
19 in my submission that are not in dispute are as
20 follows: first of all there is no record as to how
21 much in fact was used on those wards during the nine
22 month period. Secondly -

23 THE COMMISSIONER: Well, we can certainly
24 make an educated guess because we know the number
25 of patients that we have. We know the number or at
least some proportion of those patients would be on



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digoxin. We know what the average -

MS . CRONK: Could I help you, sir,
with that?

THE COMMISSIONER: If you can.

MS. CRONK: No, I can't. There is no
evidence before you, sir, as to the total ward population
on both wards throughout the entire nine month period.
There is evidence before you as to the number of
mortalities.

Mr. Commissioner, I know the number
of beds there were in that Hospital and I have heard
complaints that they were overcrowded and under-
staffed and all the rest of it and I can make, I was
going to say educated, but let's say uneducated guess
of the quantity. All you have to do is look up these
babies to know how much digoxin generally was being
provided to them. We know that most of these children
were on digoxin and then we can assume that most of
the children that were in the cardiac ward were on
digoxin.

MS. CRONK: May I suggest a number of
difficulties with that with the very, very greatest
of respect.

THE COMMISSIONER: All right.

MS. CRONK: No matter what number you



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2 assume is a total population in both wards, and
3 whether you get this by using the number of beds or
4 whether there are other figures you use, we do not
5 have evidence, sir, as to the number of those children
6 who were, for example, on intravenous digoxin
7 versus oral digoxin, and the split there obviously
8 is material.

9 We do know there is evidence that a
10 great number of children on those two wards took adult
11 intravenous digoxin both (a) because of their age and
12 secondly as Mrs. Radojewski has testified because
13 sometimes it was used by the nurses because it was
14 easier.

15 THE COMMISSIONER: Please don't mis-
16 understand me. I don't want an exact figure. I just
17 wanted to have some idea whether the amount that would
18 be required to poison these children, assuming they
19 were poisoned, would have been noticed under the
20 system that they **had** anyway.

21 MS. CRONK: Well, I can tell you two
22 things, sir, about that. The first is - this is not
23 a direct response - it wasn't. I can tell you secondly
24 if you accept the theory, for example, of Drs.
25 Kauffman and Hastreiter on some of his evidence before
you as distinct from the preliminary hearing, that we



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2 are not talking about large amounts of the drug.

3 THE COMMISSIONER: Yes.

4 MS. CRONK: If, however, you accept the
5 theory of Dr. Hastreiter's steady state amounts of
6 drug, we are talking significantly more of the drug.
7 Significantly more ampules. I don't mean, sir, not
8 to be responsive directly, but it does depend on which
9 theory of dosages you in the end accept as being the
10 most reliable and credible.

11 So that we are in a situation then,
12 sir, where although Mrs. Radojewski felt that an increase
13 would be observed after September, 1980, the ward
14 pharmacist and her assistant who testified at the
15 preliminary hearing indicated that they did not in
16 fact know the amount of digoxin that had been used
17 on Wards 4A/4B after September, 1980, and moreover
18 they did not know whether the amount used after March
19 1981 represented an increase or a decrease in the
20 amount that had been used during the inquiry period.
21 So although Mrs. Radojewski thought it likely they would
22 have noticed, her evidence is is that they in fact
23 didn't know how much was used and didn't know whether
24 after the end of the inquiry period the amount had gone
25 up or down and obviously then didn't know whether it
was up or down during the inquiry period.



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2 The effect of this evidence in my submission
3 Mr. Commissioner, as a whole is to establish the
4 following: first, that access to digoxin on Wards
5 4A/4B at least by hospital personnel during the
6 inquiry period was effectively unlimited in a recording
7 sense with no procedures in place to record how
8 much was used in either of the two wards or how much
9 was borrowed from other wards in the Hospital.

10 Secondly there is no record available
11 of how much digoxin in fact was used on Wards 4A and 4B
12 during the inquiry period, nor do we know if it was
13 an increase or decrease over amounts observed in the
14 past because the records are simply not available.
15 They do not exist. They no longer exist, I should say.

16 Thirdly, adult ampules of digoxin were
17 readily available on both wards. Inasmuch as there
18 were any number of older patients Nurse Radojewski
19 has testified that adult ampules could be used to
20 give larger doses of digoxin to younger patients,
21 and we have heard evidence as well that some of the
22 older children on the wards received their digoxin
23 in the adult form.

24 And then fourth, sir, in my submission,
25 it is probable that digoxin was not on the crash carts
on Wards 4A and 4B even on an isolated occasion during



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2 the inquiry period unless placed there either by
3 accident or by design.

4 Finally, sir, dealing with the
5 rules and procedures that applied for the administration
6 of the drug during this nine month period, I think
7 in my submission it can be shortly summarized: first
8 excluding arrest situations leaving them aside for
9 the moment, nurses on 4A and 4B according to Nurse
10 Trayner gave medication 99 per cent of the time while
11 physicians gave it 1 per cent of the time. That is
12 medications generally, sir. That is found in Volume
13 136, page 1236.

14 Secondly, in practice we have heard
15 from a great number of witnesses Registered Nursing
16 Assistants did not administer medications of any
17 kind on Wards 4A and 4B including digoxin. I refer
18 you, sir, specifically to the evidence of Carol Brown,
19 Elizabeth Radojewski, Marianna Christie and Janet
20 Brownless Two Registered Nursing Assistants who were
21 members of Mrs. Trayner's nursing team, the one on a
22 full time basis, Mrs. Christie, and one on a floating
23 basis, Miss Brownless, have both testified that on
24 no occasion during the nine month period did they
25 administer a medication of any kind and certainly did
not administer digoxin on their evidence.



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Thirdly, sir, if medications were required to be given to a patient for whom a Registered Nursing Assistant was caring a Registered Nurse would be assigned and would assume the duty of giving the medication. Very often the team leader on duty would assume that responsibility. That is the evidence, sir, of Mrs. Trayner, Miss Costello and Mrs. Radojewski.

Fourth, at the Hospital for Sick Children during the inquiry period Registered Nurses could administer digoxin orally, and by that, sir, I mean they were permitted to do so and the practice was that they did do so but they were not permitted to administer digoxin intravenously.

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In practice, they never administered digoxin intravenously on either of those two wards, according to all of the nursing witnesses that appeared before you. They could and did, however, administer other medications intravenously, so long as it was done above the buretrol on the intravenous apparatus.

Fifth, sir. I would refer you, in addition, to the oral evidence, sir, of the nursing witnesses and, with respect to the last point, to Exhibit 291, which is the Policy and Procedures Nursing Manual from the hospital in Sections 14, Sub 13; 18, Sub 1 and 16, Sub 6.

Fifth, sir. When a registered nurse gave an oral dose of digoxin on either of the two wards, she was required to have the calculation of the dose and the amount checked with a second nurse. That was required, both by the nursing manual and we have heard, sir, from nursing witnesses, including Miss Costello and Ms. Radojewski and Carol Brown, that was, in fact, the practice as it applied in the real world, if I can put it that way, on Wards 4A and 4B.

Sixth. The second nurse checking the calculations in the amount of the drug was required to be physically present when it was



EE2

1 prepared, but not when it was given. The second
2 nurse acting as the check, if you will, was not
3 required to sign that the drug had been drawn up or
4 given. The nurse administering the digoxin was
5 required to sign that it had been given on the
6 medication treatment record of the particular
7 patient in their medical chart, but was not obliged
8 to sign any overall record kept in the medications
9 room, those applied to controlled and narcotic drugs
10 and did not apply to digoxin at the time.

11 Seven, sir. A nurse drawing up an
12 intravenous drug, those that she was permitted to
13 administer intravenously, was not required to check
14 it with another nurse, save - I'm sorry, in the
15 categories of things such as ampicillan, gentamicin
16 and antibiotics. We have heard evidence from Miss
17 Bucci, sir, that heparin could be administered by
18 registered nurses, but that the practice was that it
19 would be checked by a second nurse and that, indeed,
20 is provided for in the nursing manual.

21 THE COMMISSIONER: Heparin is a blood
22 thinner or something?

23 MS. CRONK: It is an anticoagulant, sir.

24 THE COMMISSIONER: Yes.

25 MS. CRONK: You will recall, sir,



EE3

1 that heparin is a medication of more than passing
2 interest in the case of Stephanie Lombardo. That
3 was the only medication she was on prior to her
4 death.

5 Sir, unless there are any further
6 issues with respect to the actual rules that apply
7 to the administration of the drug, those are all my
8 submissions in that regard.

9 There is one housekeeping matter, if
10 I may. It arises from the transcript yesterday at
11 page 379, sir, of Volume 149. The discussion with
12 respect -- I'm sorry, page 379. The discussion with
13 respect to the relationship between high potassium
14 levels and high digoxin levels is set out and the
15 first sentence reads: "The issue as to whether or
16 not the high potassium levels can cause high digoxin
17 levels is important because Doctors Kauffman and
18 Spielberg have suggested that they think that
19 proposition to be a legitimate one." That is an
20 error, sir. It was Doctors MacLeod and Spielberg.

21 I may have misstated myself
22 yesterday and if I did, I apologize. It was clearly
23 Dr. MacLeod's evidence and Dr. Spielberg's evidence.

24 Sir, I thank you for your patience.
25 Those are all my submissions.



EE4

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THE COMMISSIONER: What do you want to do with all these charts and things? Do you want them to be exhibits or just keep them?

MS. CRONK: I don't think they need be exhibits, sir. They were really provided in the hope that they would be of assistance throughout argument.

THE COMMISSIONER: All right.

MS. CRONK: I am told that Mr. Lamek will require just a moment or two to change the guard and it seems that I have finished right on time.

THE COMMISSIONER: 20 minutes.

MS. CRONK: Thank you.

Miss Cecchetto: Perhaps it would assist if they were exhibits if other Counsel are going to refer to them.

THE COMMISSIONER: I think what we will do is put them in whatever order and make them one exhibit.

MS. CRONK: That's fine, sir. The first one, I think, then, sir, is the list of children for whom there is no post mortem data available, the 14 children.

THE COMMISSIONER: The 14 children,



EE5

1 yes. The second one?

2 MS. CRONK: The second one, sir, is
3 the list of ranges.

4 THE COMMISSIONER: Can we put the
5 index to submissions? What about that?

6 MS. CRONK: Not even I am that
7 immodest. I think perhaps that can remain not
8 formally on the record.

9 MR. BROWN: I think that should go
10 in and Ms. Cronk should be sworn.

11 THE COMMISSIONER: I agree. I think
12 that should go in, too. I think it will be helpful.
13 Then, the list?

14 MS. CRONK: The list of 14 children
15 the next and then the list of ranges, sir,
16 the toxic and therapeutic ranges set out by
17 Mr. Cimbura.

18 THE COMMISSIONER: Yes.

19 MS. CRONK: Then the list of charts
20 disclosing the actual concentrations of digoxin
21 measured.

22 THE COMMISSIONER: Yes.

23 MS. CRONK: That is it, sir.

24 THE COMMISSIONER: Maybe I have two
25 things of the ranges.



1
2 MS. CRONK: I am informed by Ms.
3 Fineberg that you have a duplicate copy.

4 THE COMMISSIONER: Thank you.

5 MS. CRONK: There will be a final
6 exhibit to be added to that, sir, when the charts are
7 ready and that is the charts recording the various
8 estimates made by the pharmacologists.

9 THE COMMISSIONER: 423.

- 10 --- EXHIBIT NO. 423: (a) List of 14 Children for
11 Whom there is No Post Mortem
12 Date.
13 (b) List of Toxic and Therapeutic
14 Ranges of Digoxin Levels Set
15 Out by Mr. Cimbura.
16 (c) List of Charts Disclosing
17 the Actual Concentration of
18 Digoxin Measured.

19 MS. CRONK: Thank you very much, sir.

20 THE COMMISSIONER: Thank you.

21 --- Short Recess.

22 --- On resuming.

23 THE COMMISSIONER: Yes, Mr. Lamek.

24 MR. LAMEK: Mr. Commissioner, before
25 I continue with the argument, I have now received
a copy of the signed Order-in-Council amending
the original Order-in-Council. I would ask that
that be substituted for the unsigned copy that we
filed yesterday.



1
2 THE COMMISSIONER: All right. I am
3 told that none of us will ever check it, but
4 probably there is a vast difference and there is
5 something in there. We will assume this is what they
6 said it was.

7 Yes, all right.

8 MR. LAMEK: Thank you.

9 Mr. Commissioner, I am turning now
10 to the individual deaths and making submissions as
11 to each child. The difficulty in dealing with 36
12 cases like this is really in determining how to
13 organize and to arrange them so as to make the
14 discussion most comprehensible. I have heard it
15 said that any order is preferable to none. This
16 isn't this case, in my view, that chronological
17 or even alphabetical arrangement is going to be
18 particularly helpful. the true problem is that in
19 many important respects the cases differ so very
20 markedly from each other. For our purpose perhaps
21 the most important difference lies in the varying
22 kinds and degrees of toxicological data that are
23 available in respect of different babies. As you
24 know, sir, the range runs from absolute zero to
25 cases such as Adamo and MacDonald and so on, right
through to a very complete one as in the case of Cook.



1 from whom we have both ante mortem and post mortem
2 serum levels in concentrations in fresh tissue.

3 If one thing is clear, it has to be
4 this: that if you are to characterize each of those
5 deaths, you must be able to rely on matters other
6 than toxicological and pharmacological data.
7 Otherwise you will be in a position with many of
8 these children of throwing up your hands in despair
9 and saying there is no way I can make a
10 determination as to the way in which the child died.

11 In many cases, and indeed in most
12 cases, the conclusion that you come to as to how
13 and by what means a child died, will be a matter of
14 inference drawn from a whole host of information.

15 I said yesterday morning that it
16 would be my submission to you, as indeed it is, that
17 a circumstance that is of enormous importance in
18 the drawing of any inference about the cause of
19 death of any child, is whether any child could be
20 shown to have died as a result of a deliberate
21 administered overdose of digoxin. I said, and I
22 say again, that if you are satisfied that even one
23 child came to his or her death in that way that has
24 to be a fact of great significance in the inferences
25 you may choose to draw in less clear cases.



1
2 Clearly the fact is of even greater
3 significance if you are able to conclude that
4 several children so died, but in my submission it is
5 true, even if there were only one, because even if
6 you don't find clear evidence of deliberate overdose,
7 causing one death, it is difficult to believe that
8 that child was the only one of 36 to have suffered
9 that fate and that the epidemic of deaths on the wards
10 is otherwise unexplained or totally innocent.

11 Had the number of deaths from July of
12 1980 until March of 1981 been within or even close
13 to the range to be expected on the basis of historic
14 experience in the hospital, a conclusion that one
15 of the deaths had been caused by deliberate overdose
16 would not make one automatically suspicious that
17 each of the other deaths was so caused to anything
18 like the degree that it must here, because in that
19 situation with a normal predictable level of deaths
20 one would start with the reasonable expectation that
21 the number of deaths that actually occurred would
22 naturally occur. Here, however, quite apart from
23 patterns, associations and common threads, the sheer
24 number of deaths, the magnitude of variation from
25 what could normally and reasonably been expected,
the epidemic of death, as it is called, demands an



1
2 explanation.

3 The conclusion that even in one case
4 there was some sinister intervention that caused
5 death has, in my submission, to trigger the
6 suspicion that similar interventions may have
7 occurred in a sufficient number of other cases to
8 explain wholly or in part the explosion in the
9 mortality rate.

10 Now, bringing this back then to the
11 question of how to approach an analysis of the 36
12 deaths, it has seemed to me that I should begin with
13 the strongest case for deliberate digoxin overdose
14 and, in my judgment, that is the case of Justin Cook.

15 If you are satisfied that Cook was
16 indeed a case of death, resulting from deliberate
17 overdose, you will perhaps, and in my respectful
18 submission, you should, give weight to that
19 conclusion in considering other more ambiguous
20 cases, and equally if, on the other hand, you are
21 not satisfied that even Cook met his death at the
22 hands of a killer, that, too, will be a very
23 important conclusion that you will carry into your
24 consideration of other deaths.

25 Let me turn then to the case of
Justin Cook.

Beyond all question, Justin Cook was a very sick baby. The cardiac anomalies were many and they were various and his hold on life was precarious. The very night of his arrival at the Hospital for Sick Children, he was taken to the ECHO Lab. The next day, a Saturday, he underwent a cardiac catheterization and surgery was scheduled for Sunday morning. All of this is the clearest possible indication of the seriousness of Justin Cook's clinical condition.

The fact that Justin Cook died before he could reach the Operating Room is not, per se, surprising. His death was certainly consistent with his clinical status and so said all the physicians. Now, it is perhaps chilling to think that if Dr. Kostigan, Dr. Coutts, had not been curious and concerned to follow up questions raised by Baby Pacsai only ten days earlier, Justin Cook's death would almost certainly have been accepted as natural, so serious was his clinical condition, but the seriousness of his clinical condition, although clearly true, is, in my submission, totally irrelevant. The overwhelming weight of the medical evidence has been that Justin Cook died of digoxin intoxication.



1
2 I refer you in that regard to Dr. Rowe
3 in Volume 18 of the transcript at pages 3724, -25;
4 Dr. Freedom, Volume 29, page 5539 and Dr. Fowler,
5 Volume 32, pages 6099 - 6100 and to Dr. Hastreiter,
6 Volume 75, pages 6588 -9. The cardiologists really
7 had no doubt about the questions.

8 The pharmacologists were a little
9 more guarded. The majority view there was that
10 digoxin may have contributed, indeed may have been
11 the major contributor to the death of the child.
12 The reference there, sir, to Dr. Spielberg, Volume 54,
13 page 2140 - 2141.

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Dr. MacLeod in Volume 63, pages 4160, 4166 - 4167; Dr. Kauffman in Volume 70, pages 5489 to 5490 and 5494. Finally Dr. Mirkin, Volume 87, pages 8873, 8881 to 8883.

We heard from pathologists too, they were clearly of the view that digoxin toxicity was the cause of death. Dr. Cutz in his case at the preliminary hearing at Volume 2, page 225; and Dr. Taylor at Volume 43, page 8807. In my submission the medical evidence compels the conclusion that Justin Cook's cause of death was digoxin intoxication.

The next issue then is how did that happen? Digoxin was not prescribed for Justin Cook. The evidence is that not only did he receive a drug which he was not supposed to have but also that he received a very substantial dose of it.

Let me start, sir, with the biochemistry and toxicology findings, and I know Miss Cronk has said something about these already today. Start with those obtained in the Hospital. Page 104 of the chart, the biochemistry report, the fourth sample from the left, the sample collected 4:30 in the morning of the 22nd of March and therefore collected before Justin Cook was pronounced dead,



FF-2

1
2 had recorded in it a digoxin concentration of
3 72 nanograms per millilitre. There is post mortem
4 serum, the next sample to the right, collected at
5 6:00 a.m., an hour after the child had died, disclosed
6 a concentration of 68 nanograms per millilitre.

7 If you were to turn, sir, and
8 I don't necessarily ask you to do so, to Exhibit 95A,
9 which is the first of the reports from the Centre
10 of Forensic Sciences, at page 1, sir, we have sample
11 T40 and T41, samples of blood, 22.3.81 which I
12 understand to be post mortem samples with a recorded
13 level of 91 nanograms of digoxin, that is calculated
14 by RIA plus HPLC and RIA. Then on page 2, specimen
15 T24 we have something that is reported to be blood
16 from Justin Cook, and the notation "no digoxin could
17 be detected in this fluid". A sample of Justin
18 Cook's serum T27 drawn at 6:00 a.m., 46 nanograms.
19 Specimen T34 red blood cells 79 nanograms of
20 digoxin.

21 Back on page 1, having seen then
22 the samples of ante and post mortem blood, we have
23 fresh tissue samples T42 and T43, heart, muscle
24 and lung and the levels have been discussed previously
25 on many occasions. In my submission the significance
of those fresh tissue concentrations is threefold.



FF-3

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2 First and most obviously the recorded levels in
3 the heart and lung are in the top parts of the
4 ranges reported in the literature as having been
5 measured in the organs of cases of fatal poisonings,
6 and the pharmacologists agreed that Mr. Cimbura
7 had correctly stated those reported ranges from the
8 literature.

9 Second, they demonstrate that a
10 considerable distribution of digoxin to tissues
11 had taken place by the time Justin Cook died and
12 that particularly in light of the impaired circulation
13 of blood from the time of arrest and during the
14 resuscitation effort precludes in my submission
15 the possibility that Cook received digoxin after,
16 at the time of, or even immediately before the time
17 of his cardiac arrest at 4:20.

18 And the third significance I suggest
19 is that the fresh tissue levels when compared with
20 the levels recorded in fixed heart and lung tissue,
21 and I refer to T11 on page 2 of that same report,
22 graphically demonstrate the degree to which dig.
23 concentrations may be reduced in fixed tissues. Fresh
24 heart tissue yielded a level of 1177 nanograms per
25 gram. If you look across the page, sir, to T11 at
the top, ventricle, left atrium and septum recorded



FF-4

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2 respectively concentrations of 8 nanograms, 39
3 nanograms of dig. and dig.-like substances and
4 4 nanograms of digoxin, and the lung which in
5 fresh tissue had been 153 was now in fixed tissue
6 15, a very dramatic reduction of the kind demonstrated
7 by Mr. Cimbura in his own laboratory tests.

8 We have with respect to Cook a very
9 complete set therefore of toxicologic data. The
10 size of dose, the time and route of administration,
11 to produce those levels in serum and fresh tissues
12 are matters on which the pharmacologists opined
13 and those views have been summarized by Ms. Cronk
14 and I won't repeat them.

15 The burden of the expert evidence
16 is that baby Cook received an overdose variously
17 described as massive, that was Dr. Hastreiter;
18 enormous, Dr. Kauffman; substantial, Dr. Mirkin;
19 very, very large, Dr. Spielberg.

20 It is my submission that the conclusion
21 is unavoidable that that overdose was deliberately
22 administered. Essentially I come to that conclusion,
23 sir, really by a process of exclusion of any other
24 possibility. I base it on four grounds. First
25 Miss Cronk has referred you to the expert pharmacological
opinion as to the probable size of dose and the time



FF -5

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2 of administration, route of administration. I
3 won't repeat all of that but I may appear to refer
4 to some of it.

5 Drs. Spielberg and MacLeod's best
6 view, as I understand the evidence, was that
7 something less than one adult vial or ampule was
8 the most likely amount administered, and that the
9 time of administration by IV bolus injection was
10 about half an hour or a little more before death.
That is to say in the period from 3:45 to 4:25.

11 It is essential to recognize of
12 course that in making those estimates the
13 pharmacologists were working with only one known
14 piece of information, two known pieces of information,
15 in this case the serum and tissue level. They
16 were attempting to arrive at two unknowns, the size
17 of the dose and the time of administration based on
18 one known and an assumed route of administration.
19 The two unknowns of course are interdependently
20 variable. That is to say the longer the period
21 between administration and death, the larger the dose
needed to produce the recorded serum concentrations.

22 THE COMMISSIONER: I'm sorry, would
23 you say that again?

24 MR. LAMEK: Yes. The longer the period
25



FF-6

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2 between administration and death the larger the
3 dose needed to explain the recorded serum
4 concentrations, because immediately after intravenous
5 injection the level in blood starts to drop and
6 distributes itself to the tissue and therefore let
7 us say a level of say 70 immediately after
8 intravenous injection may be produced by a relatively
9 small amount of digoxin. A level of 70 two hours later
10 after there has been considerable distribution has
11 to have been produced by a larger dose.

THE COMMISSIONER: That's fine.

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FF-7

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2 MR. LAMEK: Because the two are
3 interdependently variable in that way it follows
4 I suggest whichever of the unknowns is first
5 determined or assumed affects the solution of
6 the other unknown.

7 The exercise as I understand it is
8 this. If we have a serum concentration of say
9 70 nanograms per millilitre, then the total serum
10 in the body is calculable by multiplying the body
11 weight by an assigned average volume of weight of
12 serum per kilogram, and therefore the total amount
13 of digoxin in serum would be worked by multiplication,
14 the total volume of serum multiplied by concentration
15 of digoxin. The question is how far along the
16 distribution curve did the recorded serum level
17 occur. The further along the curve, the higher
18 the numerical value you ascribe to that notional
19 volume of distribution.

20 As I understand the exercise that
21 the pharmacologists go through, they have to select
22 a point on the distribution curve which is compatible
23 with the amount of known distribution to tissue
24 that has taken place, as evidenced by the recorded
25 tissue concentration, and it is a matter of judgement.

Drs. Spielberg and MacLeod selected



FF-8

1
2 a volume of distribution of 1 litre per kilogram
3 as representing in their view an appropriate point
4 on the distribution curve.

5 Dr. Kauffman considered 1.3 litres
6 per kilograms more appropriate. The point is that
7 the selection of their volume of distribution since
8 it acts as a multiplier in the formula is influential
in the calculation of the size of the dose.

9 Drs. Spielberg and MacLeod using a volume of
10 distribution of 1 litre per kilogram thus produced
11 a dose of something less than one adult ampule to
12 produce the Cook serum level, 350 to 380 micrograms
13 $\frac{3}{4}$ of an ampule.

14 Dr. Kauffman of course using a
15 higher volume of distribution produces by his
16 calculation a dose of not less than and probably
17 larger than one adult ampule. Of course as I have
18 said that selection of volume distribution bears on
19 or reflects the likely timing of the dose in the
20 judgement of the pharmacologist, the larger the
21 volume of distribution the larger the calculated
22 dose will be and the greater the assumed interval
between administration and sampling.

23 So it is Dr. Kauffman's opinion that
24 the likely dose was greater than one adult ampule and
25



FF-9

1
2 somewhat less and 8, with a likely time of
3 administration 1 to 3 hours before the time the
4 sample was drawn which yielded the ante mortem
5 concentration. A time of administration between
6 1:30 and 3:30 in the morning in other words.

7 It is Dr. Kauffman's view that
8 0.5 milligrams of digoxin, that is to say one adult
9 ampule, the dose which he calculated as the minimum
10 to produce the result, is not a feasible dose to
11 consider. His evidence at Volume 71, page 5563 to
12 4, is that that minimum dose assumes sampling
13 immediately after IV administration without any
14 distribution, but that clearly was substantial
15 distribution from the fresh tissue concentrations
16 and therefore he says the dose has to be greater than
17 .5 milligrams and given earlier than immediately
18 before sampling.

19 Dr. Hastreiter at Volume 76, pages
20 6633 - 6634 concluded that the probable dose was
21 between .8 milligrams, that is to say slightly less
22 than two adult ampules, 1.2 milligrams slightly more
23 than two adult ampules and fairly falls within the
24 range prescribed by Dr. Kauffman.

25 Now the significance of all of that
for the present purpose of course is this. In the



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first place even Dr. Spielberg agreed that if more
than one adult ampule was required as the dose
to produce the recorded levels in Cook, the
chance of that having been administered by error
is very much smaller than if one ampule or less were
required.

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2 Second, because by anybody's
3 calculation the dose that was required to produce the
4 level in Cook approximated not less than three-
5 quarters of an adult vial it cannot reasonably be
6 suggested that Justin Cook received another patient's
7 digoxin dose by mistake.

8 Now even if it were physically possible
9 that a child on constant care, for him to receive a
10 dose destined for some other child, no other child
11 would be receiving a dose of digoxin of the size that
12 Justin Cook received in the judgment of pharmacologists.

13 For that to have occurred it would
14 either mean that that dose had been deliberately
15 intended for some other child or that some horrendous
16 quadruple error had occurred; someone in preparing a
17 dose for another child had used the parenteral and
18 not the oral preparation of the drug, that he or she
19 had used the adult parenteral preparation of the
20 drug, had made a gross mistake in the size of the
21 dose and had then given it to the wrong child:
22 Cook.

23 In my submission that is so bizarre
24 as to be unacceptable as any reasonable explanation
25 for anything. At any rate one might wonder why a
child would be receiving digoxin at all between 1:30



1
2 and 3:30 in the morning; at a time at which digoxin
3 doses were normally to be administered. In my
4 submission we can rule out any thought that Justin
5 Cook received some other child's digoxin dose.

2
6 It follows, therefore, in my submission
7 that if Cook received digoxin by a mistake it could
8 only be that it was given to him in a mistake for some
9 other drug. As all of the pharmacologists agree if the
10 dose of digoxin that he had to receive was greater
11 than one adult ampule the chance that that could have
happened at all is very small.

12 Someone preparing a drug which they
13 believed to be something other than digoxin would have
14 had to break open two adult ampules to do it. So the
15 sheer size of the dose and the timing of the dose in
my submission argue compellingly against drug error.

16 There are other bases, though, for
17 rejecting medication error. My second is this: If
18 one postulates the notion that Cook received digoxin
19 instead of some other drug it is necessary to ask for
20 what drug digoxin may have been thus inadvertently
substituted?

21 It is apparent from the medication sheet
22 on page 17 of the chart that the only drug prescribed
23 for Justin Cook was Propanolol, Inderal. He received
24
25



1
2 Inderal at midnight, 4 milligrams, and you will recall
3 Miss Nelles' evidence I know that there was a syringe
4 in the refrigerator in the medications' room with 3
5 milligrams of oral Inderal already drawn up. It had
6 been placed there by Sui Scott earlier in the day.
7 There was apparently no oral Inderal in the 4A
8 medications' room.

9 That pre-drawn 3 milligrams of Inderal
10 was administered by Susan Nelles at midnight together
11 with the administration orally of 1 milligram of
12 parenteral Inderal.

13 You remember her evidence that they
14 had learned of the pre-drawn 3 milligrams of Inderal
15 when they took report, came on shift and learned that
16 from Miss Mandal, and before administering that and
17 the 1 milligram of parenteral Inderal she spoke to
18 Nurse Trayner.

19 Now it is possible - it is possible
20 that the pre-drawn material in the syringe in the
21 refrigerator was not Inderal but digoxin. In my
22 submission that is hardly likely if as Sui Scott
23 testified, and her evidence is found in Volume 118,
24 6941 to 3, she testified she drew up the drug from
25 a clearly marked bottle of Inderal on the seventh
floor. Unless of course someone had deliberately



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1
2 emptied that syringe, refilled it with 3 milligrams
3 of digoxin or the equivalent volume and left the
4 Inderal label attached to it.

5 In my submission that is a rather
6 unlikely scenario, but I will come to it. It is even
7 less likely in the atmosphere of that night I suggest
8 with the parenteral digoxin all locked up by midnight -
9 Susan Nelles had herself done that - that she in
10 selecting an ampule of parenteral Inderal had by
11 mistake picked up an adult ampule of digoxin. That
12 too in the circumstances of the night I suggest is
13 not likely to have occurred.

14 In any event none of the pharmacologists
15 is prepared to place the time of administration of
16 digoxin to Cook as early as midnight. I refer, for
17 example, to Dr. MacLeod, Volume 63, page 4196 over
18 to the top of page 4197.

19 Now in saying that I recognize, of
20 course, that the midnight Inderal was administered
21 orally to Justin Cook and presumably therefore if
22 it had been digoxin would have taken longer to achieve
23 peak effect than if it had been administered intra-
24 venously. But the dose, total dose, was .4 milligrams,
25 and as I will show shortly it is the view of the
pharmacologists that if at 3:45 a.m. digoxin had been
given instead of .6 milligrams of Inderal, that amount



1
2 still would not have produced the serum and tissue
3 concentrations recorded in Cook. And on that basis
4 it is difficult to see that if digoxin was given
5 at midnight instead of .4 milligrams of Inderal it
6 could have produced the levels that were recorded
7 at 4:30 in the morning.

5
8 So of the prescribed standing orders
9 for Justin Cook the only one known to have been given
10 to him on the night he died was Inderal at midnight.
11 No other medications were prescribed or ordered for
12 Cook until shortly before 4:00 a.m. when Dr. Kantak
13 was summoned to Cook's room.

14 He administered at that time .4
15 milligrams and then .2 milligrams of Inderal by IV
16 push to Justin Cook. As I understand the concentrations
17 of the Inderal preparation that that was a matter of
18 a total of .6 ccs of fluid.

19 It has been suggested repeatedly that
20 what was thought to be Inderal in the syringes taped
21 to Justin Cook's bed may have been digoxin. The
22 evidence is the material in one or the other or both
23 of those syringes that Dr. Kantak used at 3:50 and
24 3:55 in the morning.

25 Now may I consider for a moment the
possibility that the material in those syringes was



1
2 not Inderal but digoxin? In my submission it is
3 absolutely inconceivable that that should have happened
4 by error.

5 There were two empty Inderal ampules
6 taped to the loaded syringes. Nurse Palmar and her
7 evidence is found in Volume 40, and particularly
8 pages 2383 through to 2407, has recounted where those
9 Inderal ampules came from, how she got them, where
she got them, what she did with them.

10 She took them into Cook's room; they
11 were brown ampules. She couldn't remember the name
12 but she could certainly remember the colour. She put
13 them on Cook's bed, told the doctor who was there
14 that she had got the ampules as directed. She doesn't
15 know who drew them up in the syringes but that is what
she provided in the room.

16 In my submission it is simply not
17 possible that whoever drew up those syringes, first
18 mistook two digoxin ampules for Inderal ampules; then
19 having drawn them up presumably mislaid the empty
20 digoxin ampules, saw, picked up and attached to the
21 syringes two Inderal ampules that happened by the
22 sheerest good fortune to be lying readily to hand,
23 and then finally attached the syringes and the ampules
24 to Justin Cook's bed without ever once realizing her
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2 error. It defies reason to suggest that that could
3 have happened by accident, Mr. Commissioner.

4 Dr. MacLeod thought such an error was
5 very unlikely.

6 Now it is possible, however, that
7 someone had deliberately substituted digoxin for
8 Inderal in those syringes and had maliciously mis-
9 labelled the syringes by attaching or leaving attached
10 Inderal ampules. In that case, of course, the
11 substitution would have been deliberate and malicious
12 but the administration would have been an innocent
13 and ghastly error by Dr. Kantak at 3:50 in the
14 morning.

15 In my submission that possibility too
16 is a non-starter. The weight of the expert
17 pharmacological evidence is against it because the
18 digoxin contained in a volume of the adult preparation
19 equivalent to the volume of fluid containing .6
20 milligrams of Inderal would not be sufficient administered
21 at 3:50 and 3:55 a.m. to produce the serum and tissue
22 concentrations recorded in Justin Cook.

23 In that regard I refer you to the
24 evidence of Dr. MacLeod in Volume 66, pages 4614 to
25 5, and Dr. Kauffman in Volume 74 beginning at page
6371 and of Dr. Mirkin in Volume 88, pages 9081 to 4.



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2 In my submission there is no basis in the evidence
3 to justify a finding or even to raise a serious
4 question that the drug administered by Dr. Kantak
5 at 3:50 and 3:55 in the morning was digoxin or indeed
6 anything other than Inderal or that even if that drug
7 were digoxin it could have produced the levels
8 recording Cook's ante mortem serum and fresh tissue.

9 It is my submission, therefore, that
10 if digoxin were mistakenly administered to Justin
11 Cook in substitution for some other drug, that other
12 drug was not Inderal.

13 Now the only other known candidates
14 for mistaken substitution are those listed on the
15 chart on page 30 as having been given before 4:30
16 a.m. I say before 4:30 a.m. because that of course
17 was the time at which the sample was drawn in which
18 the digoxin level was recorded, and therefore anything
19 for which digoxin was mistakenly substituted had to
20 be done before 4:30 in the morning.

21 When I examined Dr. MacLeod I dealt with
22 these drug administrations. The evidence is found
23 in Volume 63 beginning at page 4185.
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THE COMMISSIONER: I'm sorry, what number is it did you say?

MR. LAMEK: 63, sir. Page 4185, beginning at line 16:

"Q. Now, we also know that Atropine was administered at (or) shortly after Dr. Kantak's arrival."

You will see from page 30, sir that Atropine is recorded as having been administered at 4 o'clock in the morning.

THE COMMISSIONER: Yes.

MR. LAMEK: "Indeed, if you were to turn to page 30, although that is a list of the drugs administered on the arrest it also lists the medications administered immediately prior to the arrest. We have just referred to the Inderal .4 and .2 millilitres. There was then at 4 o'clock an administration of .6 millilitres of Atropine, .1 milligrams.

Again, Doctor, you are familiar with the appearance of ampules of Antropine and of Digoxin. Is it in your view likely that there would be confusion



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"between those two ampules?

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A. There is more possibility
certainly than with Inderal, at least
the ampules are the same colour or
colourless I should say.

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Q. Yes. On the other hand if we
were to look at page 29 as you have
pointed out, the Atropine appears to
have produced a good response?"

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That is found in the note on page 29, Miss Nelles'
note, perhaps two-thirds of the way through when she
records that Atropine was given at this point with good
effect and then morphine.

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I have pointed that out to Dr. MacLeod, his answer
at line 11:

"A. Yes.

Q. What is the response that is hoped
for with atropine?

A. Well, they are looking for an
acceleration of the heart rate there.

Q. And that is not likely to have
occurred I take it had digoxin been
administered in mistake for atropine?

A. No, there probably wouldn't have
been any change in the heart rate with
digoxin. "

I take it from what we know, Mr. Commissioner, it is
unlikely that the heart would have accelerated.

"Q. Is it therefore reasonable to
infer that what was administered as
atropine in light of the noted response
was indeed atropine?

A. I think that is a reasonable
assumption."

The top of page 4187.

"Q. Now, it is also clear from page
30, Dr. MacLeod, that at 4:05 morphine
was administered, and it is not clear



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" from the chart why it was administered
and I don't know whether you have any
thoughts on that.

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A. No. I actually don't know why it
was administered; perhaps as a treatment
of heart failure which was progressive.

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Q. The child was regarded as being
very irritable, as I understand it,
and it might have been for that?

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A. Sometimes it is used to reduce
agitation.

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Q. Yes. And I tell you, doctor, upon
my review of the chart I have not found
any other order for the administration
of morphine or any other indication of
its being a PRN administration.

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A. Yes.

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Q. But I am also able to tell you from
the report of Dr. Cimbura from the
Centre of Forensic Sciences, that
morphine was found in his blood on the
drug screen that was performed at the
Centre. I ask you on that basis, is
it fair to infer that morphine was in
fact given as it was apparently intended

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to be given?

A. I think that is a reasonable inference."

Then again at page 4193, sir, beginning at line 17:

"We have looked at the drugs that were ordered and apparently administered between 3:45 and I believe, 4:26..."

And 4:26 was the last point in time that Dr. MacLeod thought -- that was the end of the period in which he thought the drug might have been administered, digoxin.

"...and there was bicarb. Only in the meantime. The only other drug that we have not yet looked at that was administered between 3:45 and 4:26 was bicarb at 4:23.

Is it likely there was confusion there, doctor?

A. I would think not. It is a rather large ampule and pretty hard to confuse. "

True enough it is that I did not ask Dr. MacLeod about the adrenaline. It was apparently administered at 4:29, one minute before the blood was drawn, in which the 72 level was found. That was because, as I say, Dr. MacLeod said in his opinion the digoxin, if it was



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2 administered, was administered sometime prior to 4:26.
3 Quite how he arbitrarily picked 4:26 I am not sure,
4 but he did. We don't know whether 2 cc's of
5 adrenaline at 4:29 could have produced the level that
6 was recorded in the sample drawn at 4:30. As to that
7 there is no evidence, Mr. Commissioner.

8 It is my submission that there is
9 no basis, no evidence to support any finding that
10 there was any medication error involving an inadvertent
11 substitution of digoxin for something else which
12 resulted in Justin Cook's receiving a sufficient dose
13 of digoxin at a time which could account for his
14 serum and tissue concentration.

15 The third basis upon which I suggest
16 there was no medication error with Cook, he was on
17 constant nursing care. Now, ironically being on
18 constant nursing care may increase his risk of being
19 subjected to foul play. I don't mean that in a
20 particular context of Cook, but any child who is in
21 the exclusive care of one or two nurses, is I suppose that
22 a greater risk if one of those nurses charged with
23 his care is given to indulging in foul play. She has
24 exclusive access to it. But on any reasonable view
25 I suggest constant nursing care must reduce the
risk of medication error. The nurse has only the one patient



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to look after. She cannot, therefore, confuse him with any other patient in the administration of medications and she will certainly know if someone else attempts to administer medication to the child while she is there.

Fourth, and last is the basis for the submission that there is no evidence of medication error, no basis for believing it could have occurred.

The weight of the pharmacological opinion did not favour accidental administration of digoxin to Justin Cook. Again, Dr. MacLeod, Volume 63, at page 4198 at line 8:

"In the light of all that you know about the sequence of events leading to this child's death and all that you know about the levels of digoxin recorded in his body, blood and tissues do you have any opinion as to the likelihood that the dosage of digoxin which this child received, whether it caused his death or not, the likelihood as to whether that dose was accidentally or deliberately administered ?

A. Yes.

Q. What is it?



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A. I imagine that it was a deliberate
overdose."

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Dr. Kauffman, the same effect in Volume 70, page
5491 and in Volume 71, beginning at 5664 and going
over to the next page.

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Dr. Spielberg thought it entirely
likely that the overdose had been given accidentally.
Dr. Mirkin expressed no opinion on the point.

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It is, therefore, my submission, Mr.
Commissioner, based upon the combined foregrounds in
which I referred, that there is no rational evidentiary
basis for any suggestion and a fortiori for any
finding that Justin Cook received a massive overdose
of digoxin by error or by accident and that one is,
therefore, driven to conclude that the overdose of
a drug which was not only not prescribed for that
child, whose use was contra-indicated, the overdose
was administered to him deliberately at some time
in the early morning hours and probably after 1:30
in the morning on Sunday, March 22nd, 1981.

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In my submission, you are entitled to
find, and indeed respectfully I say, should find that
Justin Cook died by digoxin intoxication resulting
from a deliberately administered overdose of that drug.

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THE COMMISSIONER: Thank you.



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MR. LAMEK: I have completed the submission with respect to Cook, Mr. Commissioner. May we adjourn until tomorrow morning?

THE COMMISSIONER: Yes. Can you give us some indication or can you not?

MR. LAMEK: I shall not finish tomorrow.

THE COMMISSIONER: How long do you think you would be on Monday?

MR. LAMEK: I will be through before lunch on Monday.

THE COMMISSIONER: Mr. Scott, what will your position be after Mr. Lamek finishes?

MR. SCOTT: I think we will be ready to go as soon as he is finished, at least with enough material to take us through the balance of Monday. What we are waiting to see is the extent to which we may want to cover the babies that he has already dealt with.

THE COMMISSIONER: You will be able to tell us better I guess. I just didn't particularly like the thought of bringing us all back here. I made a promise to you of giving you some time .

MR. SCOTT: Yes, I know.

THE COMMISSIONER: I didn't particularly want to --



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MR. SCOTT: At the moment I suspect we are not going to need the time and I will take the IOU to be used later in Phase II.

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THE COMMISSIONER: All right.

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MR. SCOTT: -- in order to get on with it, but perhaps if we could just leave that until we see what develops.

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THE COMMISSIONER: We can certainly give you the afternoon if you wanted to have the afternoon. I didn't like the thought of starting on Monday and then stopping and starting again on Wednesday.

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MR. SCOTT: No, I don't think we will need time of that dimension.

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THE COMMISSIONER: We will see what we get done tomorrow and we will come back Monday morning at 10:00 o'clock and hope that we will just carry straight on from there.

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All right, until tomorrow at 10:00 o'clock.

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--- Whereupon the Hearing adjourned at 4:35 p.m. until 10:00 a.m., Thursday, June 7th, 1984.

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